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An Address.[1]

By I. B. JOSE, M.C., M.S., F.R.C.S., F.R.C.S.E., F.R.A.C.S.,

President of the South Australian Branch of the British Medical Association.

IT is the purpose of the British Medical Association to further the scientific learning, to guide the public relations and to uphold the ethical tradition of the profession. It was for these purposes this Branch was formed in 1879 under the first presidency of Dr. William Gosse.

It would be presumptuous to talk to you on ethical tradition, but I consider we should occasionally give thought to some of the finer points of medical conduct which may affect us individually as teachers or as a profession. This is a time of changing social relationships in national life. These have far-reaching implications. Many affect the practice of medicine. It behoves us to see that the highest plane of professional conduct must be insisted on in the various aspects of medical life, both individual and political, if our profession is to maintain the respect, esteem and gratitude of our fellow men, and to further the future of medical practice in Australia, free from the complete control by the State of both doctors and public. This may yet depend, as it has already, on this very matter—the esteem of thinking people for those who personally help them in their ills and their desire for freedom of choice of their medical adviser in whom they have their trust.

Medical ethics contains such matters as the following, which, in the main, are scrupulously carried out by the body of the profession:

1. "The welfare of the patient above all else." This may mean loss of material gain by referring him to a person more competently trained to deal with a special condition or to make a diagnosis, or may be neglected because of personal inconvenience—with resultant indifference to answering a call for urgent help, or leaving the call to be answered by a fellow practitioner without personal request, or prearrangement if away for any time.

When a doctor undertakes to practise in an area, he undertakes the responsibility to be ready and willing to look after the sick in that area when they require his attention, or to make adequate provision for the task. Admittedly, the boot is often on the other foot. The unthinking or unreasonable request for medical attention in illness, neither acute nor urgent, at times which are customary, in this country, to reserve for leisure, must be discriminated from what I have referred to, and the experienced practitioner can do so. The beginner should not take the risk.

[1] Read at the annual meeting of the South Australian Branch of the British Medical Association on June 29, 1955.

2. The scientific ability and training of the practitioner to do what he has set himself, and his obligation during his professional life to keep abreast with scientific advances by his reading, by post-graduate instruction or by attendance at scientific meetings. It is of some concern to the Council that at all our medical scientific meetings here one is apt to see the same small group of regular attendants, but the large majority of the profession never appear unless some financial question is being discussed.

Two events have occurred in the past twelve months in this Medical School which it is expected will prepare a student better for his first impact on professional life: (i) The innovation of a short period of practitioner apprenticeship to selected general practitioners in the student course. (ii) The request to the Government for an Act compelling a year of residence before registration.

These are both steps to increase the effectiveness of a recent graduate before he is allowed to practise his art unsupervised on the public.

In this country far too much surgery is being undertaken by those who have not taken the trouble to train themselves with the very adequate opportunities that now exist to make a person competently trained. It is not always the technical ability to operate that is lacking, so much as the judgement that comes from adequately supervised experience of when an operation is necessary and how it may best be done, what varying alternatives there are and the judgement to choose the best suited to the case. In life-saving emergencies in isolated areas practitioners sometimes have to take a chance, but others should not be asked to. It is to the younger graduates I plead to plan their post-graduate training to ensure full competence in the field of work they undertake.

Let me here discuss the field of medical training, as I have had special interest in it.

Medical education must have some influence on quality of professional ethics. The conduct of the individual is based on his own character, the result of heredity and of his early upbringing, and is further influenced by his school and university life. No ideal method of pre-selection of medical students is widely accepted, except an ability to pass an entrance or matriculation examination. The elimination of the unsatisfactory is by a weeding out in the early years of the course of those unsuitable to proceed. It is important to find for these persons (not many in number) an easy diversion to another training in which the study they have done is not wasted.

The load of ever-widening avenues of factual and technical knowledge has so come to occupy the available time of the medical student that he is in danger of becoming a mere technician, of limited outlook and untrained to take his full place in life, without a knowledge of the universe and of man, or the society in which he lives. A few overcome this by natural bent and outside influences.

It is to this aspect of a medical student's early education that attention is being focused in universities throughout the world—how one can reduce the factual load and rely more on principles in the subjects of the pre-clinical part of the course, and, without lengthening the total time, allow for some wide instruction in selected subjects—literature, history, philosophy, economics. The object is to awaken the mind and to teach the student to think and reason and be well educated, rather than to fill him with easily forgotten facts. Wider study in the early years of the medical course has long been the practice in certain better Canadian medical schools, but it is largely from the influence of university life and contacts with the thought of other faculties that this may best be attained. Our Medical School is growing and has got to the stage where it needs to give, and is giving, this point further serious attention.

Other environmental influences which affect medical conduct from student days on include particularly the historical treasure of the Hippocratic Oath, the legends of the lives and work of famous physicians and surgeons, and, not the least, the unconscious influence of those who have been our teachers, and also our patients or acquaintances.

I quote from Albert Schweitzer, philosopher, musician, theologian and physician. "Much that has become our own in gentleness, modesty, kindness, willingness to forgive, in veracity, loyalty, resignation under suffering, we owe to people in whom we have seen or experienced these virtues at work, sometimes in a great matter, sometimes in a small. A thought which had become act sprang into us like a spark, and lighted a new flame within us. If we had before us those who have thus been a blessing to us, and could tell them how it came about, they would be amazed to learn what passed over from their life to ours."

The responsibility of the teacher is his conduct and example as well as his scientific attainment or ability to teach. The latter—the ability to teach—is not unimportant; and as well as trying to obtain the ideal standard of medical student, any university should pay corresponding attention to selection of at least some of their teachers for their teaching capabilities and first-rate minds. Their capability to instil the broader aspects of education I have referred to as an important part of university education.

In periods of prosperity in medicine, as in all other walks of life, there are times when the ethical is in danger of being ousted by the expedient or opportunist as a norm for conduct, both personal and political.

I now come to our professional responsibility to the State. The State, to an increasing degree, is rightly making itself responsible for availability of means to benefit the health and well-being of its citizens.

Our Australian hospital and medical benefit service and the provision of life-saving drugs have been acclaimed by responsible persons in other countries as one of the best in the world. The scheme is still in its infancy. It has many anomalies and difficulties yet to be smoothed out.

The Federal Ministry of Health and the Federal Council of the British Medical Association are in constant communication over these. The service can yet be a success, or by some be regarded as not going far enough. It cannot too often be stressed that to make it a success there must not be too great a margin of fee to be paid by the patient. The Government moiety, the insurance fund moiety and the patients' contribution, may rightly be varied by arrangement from time to time.

The general scheme leaves a great deal to the honour, the medical discrimination and the integrity of the profession—an outstanding example is the scientific use or indiscriminate use of the antibiotic drugs, which unfortunately can also become a two-edged sword, if badly used.

A consultant at the top of his professional ability has a right to charge what he considers his worth, provided that estimate is within reasonable limits. His patient in such case should be made aware of the estimate beforehand. Most consultants will forgo this when necessary to aid those in unfortunate circumstances. If not, there will be other consultants of just as good value. To the average person of average means, and this includes the great majority, it is for the medical profession and their committees to see that the margin of fee paid by the patient is not more than 10% to 20%, or the intended benefit breaks down.

It is inevitable and fair that with the Government bearing the cost and paying for the care of a gradually increasing proportion of the indigent and less wealthy, all medical fees should tend to level out, in their various grades. This would assist benefit societies in assessing their contributions.

It is difficult to speak of fees precisely in this time of rising salaries and margins for all types of work and corresponding costs. It is reasonable that the professional fees should rise equally, but when they do so medical benefits should rise with them in similar proportion. Another aspect which would enhance success is the incin-

sion of the chronically ill in the insurance benefit scheme. This is a matter which must be, and is being, worked out by the insuring societies. On the whole the profession has, by its cooperation, helped to make the medical benefit scheme an outstanding success. There has been a lot of irksome work—especially the itemization of accounts and multiple prescription writing. No Government contribution is possible without some check of this sort.

It is up to the profession, individually and collectively, through its Ethical Committees and even through State Registration Boards, to see that the action of the few does not endanger the freedom of the whole from the almost inevitable alternative — engulfment by a government bureaucracy in a government paid medical service. The pensioner benefit scheme as it is at present is an example of a fee-for-service payment. There can be no worse advertisement for a fee-for-service health scheme than the way in which a small minority have taken advantage of such service, with unnecessary supervision of the patient for their own financial gain—in a few cases in a large way, in many more to a smaller degree, a practice despicable and unworthy of the task entrusted to them.

No health service is complete without sufficient hospitals. The provision of sufficient hospital beds is a matter which in the Australian health scheme has been left to each State to develop in its own public works. This State Government has its problem with an overloaded and overcrowded public and teaching hospital, with no means test of entry, and a population increase which has demanded at least one other similar hospital, which, at last, is in its initial stages.

The Commonwealth health scheme would best be served in the immediate future in Adelaide by adding to the beds and substantially increasing the quality of medical facilities in our few better and larger private hospitals, and the gradual establishment of others. The optimum economic size of a private hospital could be from 200 to 300 beds. This means money, and the ability of controlling boards to raise it. A welcome contribution was the Government's recent offer of a small subsidy on a 50% basis to help non-profit-making hospitals overcome the immediate crisis in bed shortage.

To sit back and to say that it is too expensive to build private hospitals now and that it should be the responsibility of the Government alone, would be a step toward the eventual Government control of all hospitals with a distinct danger of full-time hospital medical service. It concerns very vitally the future and individuality of the younger of you.

We as a profession should make every effort to assist and encourage efforts to expand our private hospitals on the best level by our own example, and constantly to point out to our wealthier patients and citizens their value and the need for expanding them. Your Council has already appointed a Standing Committee on Private Hospitals with this object. This matter is a very vital corollary to the effectiveness of the Commonwealth health scheme.

In conclusion, to guide our thoughts and deeds in our professional life in the community, we should develop a philosophy of life to give standards of value and judgement.

Sir Richard Livingstone, in a recent address on medical education, insisted that a full education required this, and that though the Christian philosophy might not yet be universally accepted throughout the world, he put forward a philosophy he considered could apply to all spheres and activities of human life, in any nation or creed—the philosophy of the first-rate.

A Christian philosophy would include all this and much more. It would embrace the charge to "love thy neighbour as thyself". This might be sometimes difficult, or it might require an enormous amount of love for each neighbour. However, this could be our objective. But let us at least, in the conduct and practice of medicine, attain and hold this philosophy of the first-rate.

BLOOD CULTURE IN THE DIAGNOSIS OF LEPTOSPIROSIS IN NORTH QUEENSLAND.

By CYNTHIA J. ROSS,
Queensland Institute of Medical Research, Brisbane.

THE Queensland Institute of Medical Research established a field station at Innisfail, North Queensland, in June, 1951, to investigate "unknown" fevers. Leptospirosis has been the commonest fever recognized, and this paper reports the part played by cultural methods in its diagnosis.

Much credit must be accorded to those who pioneered the work of the field station, and were associated with it from its inception. The earlier workers, in particular Mrs. V. M. Macdonald, smoothed the way, so that material available later could be handled with a simple routine.

Methods.

Media.

Leptospiræ were cultivated in fluid and semi-solid media. Schüffner's modified base (Kelser and Schoening, 1943) and Fletcher's modified base (Mackie and McCartney, 1948), sterilized by autoclaving at 10 pounds' pressure for twenty minutes, were prepared. This pressure sterilized the media effectively, and little phosphate was precipitated. Rabbit serum, sterilized by filtration through a Seitz D9 filter pad, was inactivated in a water-bath at 56° C. for thirty minutes, and then added to the base to give a final concentration of 18% to 20% of serum. Occasionally our rabbit sera were fatty, so the rabbits are starved now for twenty-four hours before blood is taken. The final pH of the media was 7·2 to 7·4. Three millilitres of medium were dispensed aseptically into small McCartney bottles, which had been sterilized previously in the hot air oven at 170° C. for sixty minutes, and all were incubated overnight to check sterility. All glassware was washed at least five times in tap water, and finally in distilled water after detergent had been used, as traces of it may inhibit growth.

Inoculation and Incubation.

One millilitre of freshly drawn blood was inoculated at the bedside into a bottle each of Schüffner's and Fletcher's medium. Hall, Hightower *et alii* (1951) recommend inoculation with one drop of blood, but our inoculum proved satisfactory. Occasionally only one bottle of medium was inoculated. All bottles of inoculated media were incubated at 37° C. in the dark during the first twelve months, then at 29° to 30° C. A few cultures were kept at room temperature in the dark.

Field station staff could not always be present when "fever" patients were admitted to hospital, so the medical and nursing staff of the various hospitals greatly assisted this work by primary inoculation of media, supplies of which were stored at all centres. The inoculated media were forwarded to the field station, sometimes being two or three days on the journey, and incubated, as mentioned above, upon arrival.

Examination.

Cultures were examined by dark-field illumination, with the use of an eight millimetre dry objective with 8× eyepieces, seven, fourteen, twenty-one and twenty-eight days after inoculation. Those in which the leptospiræ were not found were considered "negative". Particular care was taken to distinguish between leptospiræ and artifacts (Hall, 1929). Pseudospirochætes formed rapidly in smears prepared from media inoculated with patient's blood. If leptospiræ were present, subcultures were made, and dispatched to the Laboratory of Microbiology and Pathology, Brisbane, for identification. Usually leptospiræ appeared in subculture after four days, but if they were difficult to establish, as a couple of *hyos* and *australis B* strains were, they were seeded into Fletcher's or Schüffner's medium enriched with 0·0001% nicotinic acid. All "Celledoni" strains grew well on primary isolation, but were difficult to maintain.

Contamination.

Contamination is an ever-present problem during the humid, wet summer months in Innisfail, when "mildew" flourishes even on the walls of buildings.

From experience it was found advisable to restrict air currents within the laboratory while examinations and inoculations were proceeding. Electric fans were switched off, and ventilators, doors and windows shut. The most careful aseptic technique was employed, and the work was done close to the flame of an acetylene Bunsen burner. One cotton-wool plug displaced accidentally would inevitably mean repetition of that work. All these precautions could not be taken when bedside inoculations were made; hence the rate of contamination was higher in this group.

Contamination was of two main types: (*a*) that due to yeasts and fungi (one identified as a *Penicillium* sp.) which failed to inhibit the leptospiræ (Van Thiel, 1948); (*b*) that due to motile bacilli (*Bacillus subtilis, Escherichia coli* and *Pseudomonas pyocyanea* have been identified). Leptospiræ could not be isolated if motile bacilli were present (Van Thiel, 1948; Abdoelrachman, 1947). They were seen together once, and then the leptospiræ of the *australis A* serotype died out quickly. In this series, leptospiræ were not established in seven cases, although seen in blood culture. Six of these cultures were contaminated. The wisdom of inoculating at least two tubes of medium was apparent, when it was noted that in nine instances one tube was contaminated.

Some of the contaminated cultures were purified at the Laboratory of Microbiology and Pathology, Brisbane, by intraperitoneal inoculation into guinea-pigs (Van Thiel, 1948). Blood was withdrawn by cardiac puncture thirty minutes later. This method has been used successfully a number of times since, as well as Kirschner's (1954) modification in mice.

Results.

During the period from May, 1952, until December, 1953, blood cultures from 350 febrile patients were examined in the laboratory. Leptospiræ were isolated from 77 patients. Serological evidence, based on rising titre in paired or serial samples of serum, indicated that 32 of the remaining patients suffered from leptospirosis also. The total number of cases was therefore 109. Leptospiræ were seen and culture was established in 70 cases; leptospiræ were seen but culture was not established in seven cases; culture of leptospiræ was not obtained from febrile patients (nine cultures were contaminated) in 26 cases; culture of leptospiræ was not obtained from afebrile patients in six cases.

Eleven serotypes have been isolated at the field station, and are described by Smith *et alii* (1954). Their representation in the present series is shown in Table I.

Leptospirosis affects animals as well as man. Rats in North Queensland may harbour leptospiræ in their kidneys (Cotter and Sawers, 1934). During this investigation, rats trapped in the canefields were examined. Those trapped were anæsthetized, and heart blood was collected for serological examination. Media were inoculated with small pieces of tissue from both kidneys. Impression smears made from the cut surface of the kidneys were examined by dark field illumination. In one rat—*Rattus conatus* Thomas—out of 20 examined, leptospiræ were seen in the kidney impression smears, isolated in culture, and identified as an *australis A* strain.

Some factors influencing the success of cultures are discussed below.

Number of Tubes Inoculated.

Blood from 33 patients was inoculated into a single tube of medium, and 25 leptospiral strains were recovered. Blood from 69 patients was inoculated into two tubes, usually one of Fletcher's medium and one of Schüffner's. Leptospiræ grew in both tubes in 39 cases, in one tube in 12, and in neither in 18. Inoculation of more than two tubes, as suggested by Hall *et alii* (1951), was not investigated.

A tube of Schüffner's medium and a tube of Fletcher's was inoculated from 65 of the patients. Results are analysed in Table II.

Leptospiræ were recovered in 50 cases in which blood was inoculated originally into both Schüffner's and Fletcher's media. However, only from 45 Schüffner's and from 44 Fletcher's tubes were leptospiræ isolated. Comparison of Schüffner's and Fletcher's media revealed that this difference between the two for the culture of leptospiræ was not significant when subjected to the χ^2 distribution test.

TABLE I.

Distribution of Cases Amongst the Eleven Serotypes.

Serotype.	Leptospiral Culture Established.	Leptospiræ Seen—Culture Not Established.	Culture Not Obtained from Febrile Patients.	Culture Not Obtained from Post-Febrile Patients.	Total.
australis A ..	20	1	10	1	32
australis B ..	16	1	7	2	26
hyos	6	—	1	—	7
canicola	4	—	1	1	6
icterohæmorrhagiæ ..	2	—	—	—	2
pomona	2	—	—	—	2
medanensis ..	0	—	—	—	0
"Kremastos" ..	12	—	2	—	14
"Szwajizak" ..	3	1	—	—	4
"Celledoni" ..	3	1	—	2	6
"Robinson" ..	2	1	2	—	5
Type not determined ..	—	2	3	—	5
Total ..	70	7	26	6	109

Cultures were examined weekly. The results of cultures from 39 patients can be compared with regard to the time at which organisms appeared first in either medium.

Two-thirds of the strains appeared in Fletcher's medium at the first examination, whereas only half were present in Schüffner's medium. The figures suggest that the organisms may grow a little faster in Fletcher's medium, but the difference is not statistically significant.

TABLE II.

Culture Results for Schüffner's and Fletcher's Media.

—	Results with Fletcher's Media.		Schüffner's Media: Total Positive Results.
	Positive.	Negative.	
Results with Schüffner's media: Positive	39	6	45 (69·0%)
Negative	5	15	—
Fletcher's media: total positive results ..	44 (68·0%)	—	—

Leptospiræ belonging to eight serotypes were detected at the first examination. Both "Robinson" and *pomona* serotypes were not seen until fourteen to twenty-one days. Odd individual serotypes appeared quite late; an *australis A* from Schüffner's medium, and a "Szwajizak" from Fletcher's were found at the fourth examination. Another *australis A*, not included here, was seen initially thirty-one days after inoculation.

The Stage of the Disease.

The day after the onset at which blood culture was attempted was compared for both the successful and unsuccessful cultures. The results are shown in Table IV.

Leptospiræ were isolated from 49 out of the 57 blood cultures attempted during the first three days of illness, 27 out of the 45 attempted from the fourth to the sixth days, and from only one attempted later. This was a *canicola* strain recovered from a febrile patient on the ninth day of illness.

TABLE III.
Day on which Leptospiræ were First Noted in Culture.

Medium.	Examination after Approximately			
	7 Days.	14 Days.	21 Days.	28 Days.
Schüffner's	20	16	2	1
Fletcher's	26	11	1	1

The rate of failure became progressively higher as the end of the febrile phase approached. Cultures were made from 17 patients on the last day of fever, and leptospiral strains were isolated from 10 of these—five belonged to the *australis A* serotype, two to *hyos*, two to *australis B* and one to "Kremastos".

TABLE IV.
Relation of Blood Culture to Interval from Day of Onset.

Cultures.	Day of Illness.[1]										Total.
	1	2	3	4	5	6	7	8	9	10	
Cultures made	7	23	27	25	15	5	2	1	3	1	109
Successful ..	7	18	24	16	7	4	—	—	1	—	77 (70%)

[1] Day of onset was named day 1.

The Degree of Fever.

The temperature of the patient was not always recorded when blood was withdrawn for culture, so the figures noted in Table V are the maxima on that day.

This table shows that culture was unsuccessful when the temperature was less than 100° F. The lowest temperature recorded for a patient from whom leptospiræ were isolated was 100·2° F. The organisms belonged to the *australis A* serotype. The "Kremastos" serotype caused

TABLE V.
Maximum Temperature of Patient on Day of Culture.

Cultures.	Temperature (Degrees Fahrenheit).				Total.[1]
	Less than 100.	100·2 to 102.	102·2 to 104.	Greater than 104.	
Cultures made	11	21	51	23	106
Successful ..	0	17	39	20	76 (72%)

[1] Three patients were not admitted to hospital when blood culture was attempted.

the infection in the two patients whose temperatures lay between 100·2° F. and 100·9° F. when blood culture was attempted. There was no apparent correlation between the degree of fever above 100° F. and successful culture.

In addition, blood was cultivated from two patients during a relapse. In both cases there were an elevation of temperature and a return of former symptoms. Nevertheless, cultures were unsuccessful.

The foregoing sections agree with Gsell's (1952) concept that leptospirosis is characterized clinically by an abrupt onset with an acute febrile phase, during which leptospiræmia is present. The temperature then falls by lysis, and the second phase follows. In this there is a localization of the organism in foci in various organs, and attempted blood culture gives negative results.

The Effect of Previous Leptospiral Infection.

Investigation of the "acute" serum in 109 cases in this series revealed evidence of previous leptospiral infection in nine instances. A titre of at least one in 100 was considered significant. A titre of one in 1000 against *L. hyos* was encountered, while a titre of one in 300 was met four times.

Leptospiræ were isolated from six of the nine patients. Previous infection did not therefore affect the recovery rate of leptospiræ from blood culture in a subsequent infection.

Antibiotics.

Usually antibiotics were administered to patients after blood had been withdrawn for culture (Doherty, 1955). Treatment occasionally preceded blood culture.

Nineteen patients were given antibiotics prior to the taking of blood for culture. Four were afebrile when culture was attempted, and are excluded. Leptospiræ were recovered from six of the remaining 15. This proportion is well below the general average. The figures are not large, but the χ^2 distribution test reveals that the difference is statistically significant ($P < 0{\cdot}01$).

The six strains isolated were a *pomona*, *hyos*, *australis A* and *australis B* from patients who received penicillin, and an *australis A* and *australis B* from those who received chloramphenicol. It is interesting that leptospiræ were not seen in culture until the second examination in seven of the nine tubes inoculated from these patients. The organisms were detected in other tubes at the first and fourth examinations. This indicates a definite delay, as leptospiræ were seen in 67% of Fletcher's media cultures and in 51% of Schüffner's at the first examination.

No culture was obtained from nine patients previously given antibiotic therapy. Analysis of these cases presented the following facts. One patient, whose infection had been serologically caused by *canicola* serotype, had been given 800,000 units of penicillin intramuscularly, followed by chloramphenicol, before culture was attempted. Others, with infections due variously to an *australis A*, two *australis* B and a "Robinson" strain, received penicillin intramuscularly, in a minimal dosage of 100,000 units every three hours, for at least twenty-four hours prior to attempted blood culture. A "Kremastos" strain was not grown on culture from a patient given 1·25 grammes of chloramphenicol, followed by 200,000 units of penicillin by intramuscular injection every three hours, and organisms were not recovered from two patients with *australis A* infections who had received at least three grammes of chloramphenicol previously.

Thus, administration of antibiotics adversely affects the ability to recover leptospiræ from the blood, although it may not prevent it.

Discussion.

Leptospiræ are not isolated easily. Blood culture was used here as the principal method for laboratory diagnosis of leptospirosis. The efficacy of this method can be assayed from the figures available. Leptospiræ were seen in blood cultures from 77 of 109 patients. Six patients were afebrile, so those cultures were unsatisfactory. This cultural method gave 75% efficiency. Better results would be obtained if blood was cultivated early in the febrile phase and prior to antibiotic therapy. Development of more suitable media and elimination of contamination would increase the efficiency.

Detection of leptospiræ in the culture is positive evidence of leptospirosis, irrespective of whether the organisms are isolated in pure culture or not—only the type may remain undetermined. The isolation of a strain leads to the only certain determination of the serotype to which it belongs. Serological tests are valuable; but because of co-reactions, the infecting strain may be difficult to determine. The agglutinin-absorption test (Wolff, 1953) may solve this

problem. Identification of the strain is more valuable in epidemiology than in the immediate treatment of the patient—the most important fact, both to the patient and to the clinician, is whether the patient is suffering from leptospirosis.

Most strains of leptospiræ are not seen in culture until seven or fourteen days after inoculation, so this means a long delay before the culture result, if positive, is available. The various serotypes are not morphologically distinct, so more time must elapse before identification is complete.

Laboratory animals may be infected with many leptospiral strains. Of North Queensland types, *icterohæmorrhagiæ*, *australis A*, *australis B* and "Robinson" cause a febrile and often fatal illness in guinea-pigs. An *australis A* strain caused a fatal infection in mice. However, some guinea-pigs inoculated at the Institute with *medanensis* and "Kremastos" showed no obvious signs of illness, and mice inoculated with *australis B* remained well, although they became chronic carriers. Therefore animal inoculation is not always satisfactory for diagnosis of leptospirosis in North Queensland, and this offers an explanation why recently isolated strains were not discovered earlier (Cotter and Sawers, 1934).

A quick diagnosis may be available for those serotypes which infect guinea-pigs or mice. Leptospiræ can often be demonstrated in the peritoneal fluid of guinea-pigs, approximately four days after intraperitoneal inoculation (Van Thiel, 1948). This has been confirmed; guinea-pigs were inoculated with a "Robinson" strain, and leptospiræ were seen in peritoneal fluid after four to eight days. More were inoculated with an emulsion of heart blood, liver and kidneys from the originals, and leptospiræ were seen again in the peritoneal fluid. Popp (1950) has stated that an earlier diagnosis may be made by the intraperitoneal inoculation of citrated blood into young white mice. Leptospiræ, most probably *grippotyphosa* or *sejroe* strains, were demonstrated in peritoneal exudate on the second day.

Thus, diagnosis of leptospirosis should be available in some cases two to four days after primary inoculation, but in the large majority seven to fourteen days afterwards.

Serological examination remains a most important diagnostic test, even though the result does not become positive until the eighth to tenth day (Smith *et alii*, 1954) and is often specific only much later.

Therefore no method is of immediate use to the clinician for diagnosis and treatment of leptospirosis. The laboratory tests aid by giving an accurate final diagnosis, on which the clinician can build his experience, and are valuable in epidemiological investigations and industrial medicine. Leptospirosis is an occupational hazard amongst workers, particularly canefield workers in North Queensland (Derrick *et alii*, 1954), and compensation is arranged after laboratory confirmation of the disease has been obtained.

Summary.

1. Eleven serotypes of leptospiræ caused leptospirosis in 109 human subjects. The organism was isolated from the blood in 77 of these. One rat was found infected.

2. Reasons why culture failed in the remaining cases were as follows: contamination, attempted culture from afebrile patients, attempted culture from those who had previously received antibiotics.

3. Factors associated with successful culture were the collection of blood for culture under the best achievable conditions, and inoculation of two tubes of medium with blood from febrile untreated patients.

4. An efficiency of 75% is claimed by the cultural method of diagnosis outlined in this report.

Acknowledgements.

I should like to acknowledge the assistance given by Dr. R. L. Doherty, medical officer at the field station since March, 1953, in the laboratory on many occasions. I should also like to thank Dr. I. M. Mackerras and Dr. E. H. Derrick for their help and encouragement, both during my term at the field station, Innisfail, and later in the preparation of this paper. Finally I should like to tender my thanks to all members of the staff of the Queensland Institute of Medical Research, Brisbane.

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CHEMOTHERAPY IN CANCER.[1]

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"CHEMOTHERAPY is the only approach to the treatment of cancer which offers the possibility of curing and controlling the disease *irrespective of the stage* at which treatment is instituted." (Karnofsky, 1953.) The vista thus opened by the use of chemotherapy appears boundless, but so far none of the substances used have been proved capable of effecting a cure in cancer, although the possibility of temporary control by some of the agents is now well established.

The principle of such treatment is to administer, orally or parenterally, a chemical compound which will inhibit the growth of a malignant tumour without adversely affecting the metabolism of the somatic cells. The difficulty is that the metabolism of the cancer cell is basically similar to that of the normal cell, in that normal cell division and subsequent stimulation of blood supply and of stromal reaction become exaggerated in the cancer cell. The radical difference is, of course, that instead of assuming the function of its cell of origin, the cancer cell assumes the properties of invasiveness and metastasis. So far, no chemotherapeutic method capable of controlling these latter properties has yet been developed.

The mode of action of chemotherapeutic agents can be broadly classified as follows: (i) antimetabolic activity—

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for example, folic acid antagonists, mustards, urethane, stilbamidine; (ii) damage to the vascular bed of a tumour—for example, colchicine, Coley's toxin; (iii) concentration of toxic substances in cell—for example, radioactive iodine in the thyroid gland; (iv) alteration of hormone balance—for example, anabolic effect of steroid hormones and inhibition of gonads, pituitary, or adrenal cortex by hormones or by surgery in breast or prostatic carcinoma; (v) effect on embryonic tissue—for example, vitamin B_{12} causing necrosis in neuroblastoma; (vi) necrotizing viruses—for example, Egypt 101 virus.

The anti-metabolic group, in general, exerts an effect on the mitotic activity of tumour cells by interference with the synthesis of essential nucleo-proteins. Thus the folic acid antagonists may inhibit the conversion of folic acid into the citrovorum factor and its synthesis into nucleoprotein. Similarly, urethane may compete with the natural amines in the synthesis of nucleotide, and stilbamidine may weaken critical side chain linkages in nucleo-proteins. In the case of the nitrogen mustard group, the disturbance of synthesis of nucleotides is associated with chromosome breaks also, similar to the action of ionizing radiation, and its action is thus described as radiomimetic.

The failure to obtain a cure by the agents so far used is ascribed to the development of tumour resistance. It is postulated that the agent used will destroy susceptible cells, but the surviving resistant cells will multiply and soon predominate. However, the combination of certain chemotherapeutic methods together, or with X-ray therapy, may enhance or prolong their separate effectiveness. Alternatively, it might be possible to alter the local tumour environment and thus make it relatively more susceptible than normal tissue (for example, by the effect of anoxia or the combination of "Synkavit" with X-ray therapy). Theoretically, also, it might be possible to supply a protective substance in critical dosage to protect the normal tissues alone.

So far the reticuloses have been the main group treated successfully by chemotherapy (as distinct from hormone therapy). This group of diseases must be regarded in a broad sense as neoplastic. The cellular proliferation is in the main multicentric, but the tumour behaves essentially in a malignant fashion. The members of the group will be considered individually and the benefits of chemotherapy contrasted with those of X-ray therapy.

Acute Leuchæmia.

By combined therapy, as outlined below, about 50% of patients with acute leuchæmia will survive more than one year (compared with about 5% of those untreated). X-ray therapy is not indicated.

"Aminopterin", "Amethopterin" and "Aminoanfal".

Administration of "Aminopterin" (aminopteroyl glutamic acid) can cause a temporary remission in acute leuchæmia, especially in the lymphatic type.

Farber (1948) reported that in 68% of 425 children there was a transient clinical improvement for two or more months, with regression in size of the enlarged spleen, liver and glands. Occasionally there is a hæmatological remission after three or four weeks' administration, but resistance to "Aminopterin" soon develops. At this stage ACTH or "Purinethol" may be tried.

The dosage is 0·5 to 2·0 milligrammes of "Aminopterin" given by mouth daily, but toxic symptoms consisting of ulcerative stomatitis, vomiting and diarrhœa usually develop after a few days' administration. Dosage at a maintenance level must be continued when a remission in the blood count has been attained.

"Purinethol."

"Purinethol" (6-mercaptopurine) is a purine antagonist, developed at the Sloan Kettering Institute, related to the folic acid antagonists. It is of value in the treatment of acute leuchæmia which has become resistant to "Aminopterin" (particularly leuchæmia of the monocytic type), and is considerably less toxic than the latter. Unlike the folic acid antagonists, oral ulceration is a rare complication of its use. Of 101 children treated by Burchenal (1953), 50% showed clinical and hæmatological remission lasting from two to twenty-two months after three to six weeks' administration. Of 49 adults, only 14% showed remissions, but the results in adults are still better than those obtained with "Aminopterin". The dosage is 50 milligrammes daily for children and up to 200 milligrammes daily for adults (one milligramme per pound of body weight).

ACTH and Cortisone.

ACTH and cortisone may also produce remission in the course of acute leuchæmia, possibly by stimulation of the bone marrow. The effect is much more rapidly achieved than that of the antimetabolites, but remissions are very much shorter. In about half the patients treated there are a rapid fall in temperature, improvement in appetite, and shrinkage of the spleen and of the enlarged glands, and the blood count may even return to normal. This treatment is thus indicated when the patient is acutely ill; but after one or two months, relapse usually occurs, when the condition may respond to "Aminopterin" or "Purinethol". The dosage is 50 to 100 units of ACTH per day given intramuscularly, or 100 to 200 milligrammes of cortisone given orally.

Toxic effects include a tendency to peripheral œdema, alkalosis, hypocalcæmia and glycosuria. With these signs there is no need to stop therapy; but if hypertension, mental disturbance or intercurrent infection develops, hormone therapy must be discontinued.

Blood Transfusion and Antibiotics.

According to Biermann, treatment by blood transfusion and antibiotics is said to give results equally as good as those following the use of the antimetabolites or of ACTH.

Chronic Myeloid Leuchæmia.

The average survival period in chronic myeloid leuchæmia is three to four years, whether the condition is treated or not; but the useful life of the patient is increased by relief of symptoms.

"Myleran."

"Myleran" (1:4-dimethane sulphonoxy butane) was developed at the Royal Cancer Hospital, London, in 1953. It has a more specific depressive effect upon myeloid tissue, both normal and abnormal, than upon other constituents of the marrow, and is the most effective chemotherapeutic agent in this disease.

Treatment results in reduction of the immature myeloid cells in the blood, reduction in the cellularity of the bone marrow, and rise in the hæmoglobin level and reticulocyte count after about three weeks of treatment. At the same time there are subjective decrease of malaise and diminution in the size of the spleen.

Although the toxic margin is high, large doses may depress the platelet count and cause hæmorrhagic symptoms or may lead to agranulocytosis after four to six months. The dosage recommended is six to ten milligrammes daily for one to four months, and a maintenance dose of four milligrammes daily for as long as hæmatological improvement continues. The terminal acute phase of the disease is resistant to "Myleran".

In 19 cases reported by Haddow (1953), all the patients responded initially, nine relapsed within six months, and the rest maintained remissions for up to two years. Remissions are usually longer than those following X-ray therapy.

Urethane.

Urethane (ethyl carbamate) was found to inhibit mitosis in leucocytes, particularly those of a primitive type, in myeloid leuchæmia. Treatment results in a fall in the white cell count with disappearance of myeloblasts, a rise in the red cell count and hæmoglobin level (its degree of recovery being an index of prognosis), and a rise in the platelet count. At the same time there is usually diminution in the size of the enlarged spleen.

The effect of urethane in chronic myeloid leuchæmia is thus similar to that of X rays, but remissions are generally shorter, and the rate of fall in the cellular elements of the blood cannot be so carefully controlled as by X rays. The toxic effects of the drug are usually worse, and include nausea, vomiting and diarrhœa, and there is a danger of inducing aplastic anæmia and agranulocytosis.

The dosage is two to four grammes daily, in an elixir, for two to six weeks, until the white blood cell count has fallen to 20,000 per cubic millimetre.

Cortisone and ACTH.

The administration of cortisone (200 milligrammes given orally) or of ACTH (100 units by injection) daily for two to three weeks can be employed in addition, particularly in the cases of subacute myeloid leuchæmia. This leads to subjective improvement, gain in appetite, and some shrinkage of spleen and liver while hæmatological benefit from either urethane or "Myleran" is being awaited. It also benefits the patient by its effect upon the tendency to hypersplenism, which is usually present.

Radioactive Phosphorus.

According to Lawrence (1948), the use of radioactive phosphorus led to a longer average survival than that following the use of other methods. In 250 cases of this disease the average survival period was five years. When it is given either as a single dose of five to ten millicuries or in doses of one millicurie weekly, a comparable remission to that from X rays (six to twelve months) is obtained in the early stages. However, this beneficial effect is generally lost at a later stage. P_{32} can be given intravenously in saline, or orally at a somewhat higher dosage.

X-Ray Therapy.

Treatment of the enlarged spleen by X rays will usually ameliorate the symptoms of pain and nausea due to its size more quickly than other methods—that is, within a few days. The dosage required does not lead to any radiation sickness. At the same time the white cell count falls, and associated with this fall is a rise in the red cell count and hæmoglobin levels. Remissions usually last only for six to twelve months before further treatment is required.

Other Agents.

In this disease 6-mercaptopurine has been used with success, but remission may take up to two months to achieve, and treatment must be continued even after remission has occurred. Triethylene melamine can also achieve remissions clinically and hæmatologically, but may induce unpredictable and permanent marrow depression.

Chronic Lymphatic Leuchæmia.

Triethylene Melamine.

Triethylene melamine (TEM) was originally developed for crease-proofing of clothes and showed growth-inhibiting powers on animal tissue. It is chemically related to nitrogen mustard, but leads to less gastric upset, and can be given orally. It is the most useful of all chemotherapeutic agents in chronic lymphatic leuchæmia.

In about half the patients so treated, splenic and hepatic enlargement is reduced and enlarged glands undergo diminution in size. The white cell count falls to normal levels in four to eight weeks, and the red cell and hæmoglobin levels begin to rise after this period in some of the cases. However, relapse is usual after a period of two to six months.

The disadvantage of TEM is that the effect on the bone marrow is cumulative, and depression of marrow activity may lead, after two to three weeks, to thrombocytopenia, aplastic anæmia or agranulocytosis. It may also cause renal damage with transient appearance of red blood cells in the urine and rise in the blood urea level.

Dosage is at a level of 0·2 to 0·4 milligramme per kilogram in each course—that is, 10 to 20 milligrammes in a weekly dosage of 2·5 to 5·0 milligrammes. The tablets are given on an empty stomach with sodium bicarbonate, as their activity is inhibited by the gastric secretion.

Urethane.

The effect of urethane upon chronic lymphatic leuchæmia is not as consistent as it is in chronic myeloid leuchæmia. Although the white cell count may fall and the red cell count rise after its administration, regression of the enlarged glands and spleen is not always associated.

Cortisone and ACTH.

The administration of 100 to 200 units of ACTH daily for two or more weeks will often cause striking temporary shrinkage of the enlarged glands, spleen and liver in this disease. Subjective improvement for one to two weeks is common, but there is little effect on the blood picture.

X-Ray Therapy.

Localized treatment of enlarged glands or spleen by X rays will always lead to their regression, even after small dosage, and will bring the white cell count to normal, presumably by production of leucolytic substances. This is, therefore, the preferred treatment in this disease, as there is no danger of depression of bone-marrow function such as occurs with the chemotherapeutic agents. Sometimes there is associated with the fall in the white cell count a rise in the red cell and hæmoglobin levels, but this is not consistent.

Multiple Myelomatosis.

Urethane.

Urethane is the most useful chemotherapeutic agent in multiple myelomatosis and is said to have the capacity to inhibit plasma cell growth in the disease. In a series of 66 cases reported by Haddow (1953) there resulted clinical improvement in 50%, with rapid relief of pain, gain in weight and diminution in the size of the spleen and peripheral glands. In addition there ensued regression of anæmia and reduction of abnormal serum proteins in the blood. However, radiologically, regression of bone deposits occurs in only a small proportion of such cases. There is no increase in the expectation of life, and eventually relapse occurs after one to two years' administration of the drug in the majority of cases.

The dosage is two to four grammes per day, but an attempt is made to reduce the dose as soon as possible because of the danger of aplastic anæmia, agranulocytosis and thrombocytopenic purpura.

"Stilbamidine."

Trial of "Stilbamidine" (4:4-diamidino-stilbene) in myelomatosis was based on the observation that both kala azar and myelomatosis were associated with hyperglobulinæmia. Following the good results obtained by "Stilbamidine" in the former disease, Snapper (1945) reported on its trial in 186 cases of myelomatosis. In over half the cases relief of pain occurred for a period of three to six months. After such treatment, large basophile inclusion bodies are said to appear in the myeloma cells, but there is no retardation of the multiplication of the tumour cells. Radiological recalcification of the deposit is rarely seen, and there is no change in the abnormal protein levels in the blood.

Unfortunately the toxic effects are serious, and include anæsthesia of the face followed by intractable trigeminal neuralgia in over 50% of cases after two to three months. There are usually also an immediate fall in blood pressure and tachycardia if the injection is rapid.

The dosage is 150 milligrammes given intravenously daily, the dose being repeated for about two weeks in each course, and the protein intake is restricted during treatment because of the danger of renal failure.

X-Ray Therapy.

X-ray therapy will promptly relieve the pain of localized deposits in bone in the vast majority of cases, and may

occasionally even lead to recalcification. However, it has the disadvantage that each new area must be treated as it arises. On the other hand, unlike the chemotherapeutic methods, there is no tendency to depression of the bone marrow if small areas are treated.

Polycythæmia Vera.

Radioactive Phosphorus.

Actively proliferating tissues show increased phosphorus metabolism, the uptake being particularly high in the bone marrow, spleen, liver and lymph nodes. Thus, radioactive phosphorus, which emits β rays, is able to exert selective irradiation of these tissues after being taken up. (The administration of five millicuries to a man weighing 60 kilograms is equivalent to about 30*r* of whole body irradiation.)

Remissions of polycythæmia, after such treatment, vary from three months to three years, and are more prolonged than those following other treatment. A further advantage of P_{32} over X-ray therapy is the avoidance of X-ray sickness and skin reactions. On the other hand, the blood count must be carefully watched for a prolonged period because of the more pronounced effect of the element on the bone marrow, and there is a definite danger that repeated use of P_{32} may convert the polycythæmic state into a leuchæmic state.

An initial dose of three to five millicuries is given, usually after a preliminary venesection, and the blood count is assessed after three months and thereafter at two-monthly intervals.

Triethylene Melamine.

In view of the depressant effect of TEM on hæmatopoiesis and upon the thrombocyte level, this compound has been tried in the treatment of *polycythæmia vera*. Rosenthal (1953) reports remission in the red cell count in 20 out of 30 cases for periods of eight months upwards. The full effect takes three to four months to show itself, and clinical improvement, with associated reduction in white cell count and platelet level, is associated in the majority of cases.

The dosage is 2·5 to 5·0 milligrammes every one to three days, for a total of 15 to 30 milligrammes.

X-Ray Therapy.

Irradiation of the long bones or of the thorax has been practically discontinued since the introduction of P_{32}. Remissions following X-ray therapy are shorter, as the effect on the marrow is less prolonged.

Hodgkin's Disease and Reticulosarcoma.

Nitrogen Mustard.

The use of nitrogen mustard (methyl-bis-chloroethylamine hydrochloride) in the treatment of the reticuloses resulted from the observation that mustard gas had a depressant effect on mitosis in lymphoid tissue and the bone marrow. In addition, the susceptibility of tissues to its lethal effect depends upon their rate of mitosis. The administration of nitrogen mustard induces chromosomal abnormalities, and this process leads eventually to cell death. Long-continued administration will thus result in lymphatic atrophy and aplasia of the marrow.

The *bis* compound is less toxic than the *tris* compound, and a good response is obtained in Hodgkin's disease, in reticulum-cell sarcoma, in giant follicular reticulosis, and in *mycosis fungoides*. The best results have been observed in Hodgkin's disease, although in the other diseases occasional short remissions have been obtained. In Hodgkin's disease, glandular and splenic enlargement is controlled in the majority of cases. Pyrexia, pruritus or other manifestations of disease activity can be inhibited, and a concomitant improvement of the general condition is common.

The total dosage is 0·4 milligramme per kilogram of body weight, and this is usually administered in four fractions at daily or weekly intervals. The solution must be freshly prepared, and is injected into a saline intravenous drip apparatus, as tissue necrosis may ensue if there is leakage outside the vein. Toxic effects include immediate nausea and vomiting, which may be controlled by a preliminary injection of "Pyridoxin" or "Largactil". There is often a fall in the lymphocyte, granulocyte and platelet levels after one to two weeks, but the fall in the erythrocyte level is later because of the erythrocyte's relatively longer life. A preliminary leucocytosis is occasionally seen. The blood count returns to normal three to four weeks later, but cortisone may be necessary as a marrow stimulant if recovery is slow. Although recovery of hæmatopoiesis occurs sooner after nitrogen mustard than after X-ray therapy, with repeated courses of mustard marrow depression is severe and the white cell count becomes lower each time. Clinical remissions are also shorter than those following the use of X rays, and the compound cannot be applied locally for the treatment of a localized gland mass. Thus X rays have the advantage in early cases. However, nitrogen mustard treatment is useful for acquired resistance of deposits to X-ray therapy or for skin atrophy over a gland mass preventing further irradiation. It is also useful in the generalized phase of the disease with pyrexia and multiple gland masses, and for generalized pruritus possibly associated with a hidden paraaortic gland mass.

Chemotherapy of Advanced Cancer.

Folic Acid Antagonists.

"Aminopterin" and "Amethopterin" have been tried extensively in advanced cancer of all types. Clinical regression has been demonstrated in such varied conditions as breast carcinoma, seminoma and rhabdomyosarcoma, with metastatic involvement, but such regression is temporary. The dose level must be just below that capable of inducing the earliest toxic symptoms.

Most patients will tolerate two milligrammes of "Aminopterin" daily for five days, but usually a rest of one week is necessary before a further course can be given. The toxic symptoms of "Aminopterin" are marked, with ulcerative stomatitis, nausea, vomiting, abdominal pain or diarrhœa. Bone marrow depression is seen in the large majority of cases, with leucopenia, thrombocytopenia and anæmia.

Azaserine.

Azaserine, an antibiotic isolated from streptomyces culture, has been found to inhibit the synthesis of purines in the cell, its action being similar to that of 6-mercaptopurine. It has been found to induce brief remissions, particularly in some cases of reticulosis, but toxic symptoms develop usually after one to three weeks of administration, with unpredictable oral ulceration, leucopenia or jaundice.

Guanozolo.

Guanozolo (8-azaguanine) was found to inhibit the growth of adenocarcinoma in mice, and has been used in the treatment of disseminated malignant disease. Toxic effects, both generalized and local, are severe, and remission in the malignant process is only rarely obtained.

Nitrogen Mustard and TEM.

Both nitrogen mustard and TEM have been used in the treatment of inoperable carcinoma of the bronchus. In the case of nitrogen mustard the dosage is 0·4 milligramme per kilogram, given intravenously in four divided daily doses (that is, five to seven milligrammes daily). In the case of TEM the dosage is five to ten milligrammes per week, given orally, for three to four weeks. Relief of symptoms, such as hæmoptysis, pain in the chest, cough and dyspnœa, is commonly noted, even if mediastinal obstruction is present. Although there is no definite prolongation of life, it is certain that the useful life of the patient is prolonged. The final deterioration is then rapid and merciful.

Other malignant tumours, especially fibrosarcoma and neuroblastoma, have shown temporary regression following the use of nitrogen mustard or TEM. Nitrogen mustard in

these cases is often given intraarterially in order to obtain high concentration of the compound in a particular region—for example, into the femoral artery for sarcoma of the thigh, into the iliac artery for pelvic tumour, or into the carotid artery for a brain tumour. It is interesting to note that, in the last instance, there result epilation and erythema in the area supplied, similar to that following X-ray therapy.

Triethylene Phosphoramide.

Triethylene phosphoramide (TEPA) is related to TEM and has shown some favourable results in the treatment of disseminated neuroblastoma and malignant melanoma. Of nine cases of neuroblastoma reported by Farber (1953), in four there was regression of the tumour for about two or three months, and of eight cases of malignant melanoma, in two the tumour regressed. However, toxic symptoms include leucopenia and thrombocytopenia in about half the cases after about two or three weeks' administration. The reported dosage varies, but the average is five to fifteen milligrammes weekly.

Vitamin B_{12}.

Spontaneous necrosis is occasionally seen in neuroblastoma, and occasional untreated patients survive for ten years or longer. Occasionally also, spontaneous maturation to ganglioneuroma is seen in one portion of a neuroblastoma. Intramuscular administration of vitamin B_{12} at a dosage level of 1000 microgrammes on alternate days for up to two years has been reported to induce striking regression of the primary tumour and metastases in several cases. Histologically, necrosis and not maturation was found in these cases, and it is problematical whether the action of the compound is by direct metabolic interference or by the induction of growth in excess of the blood supply.

Necrotizing Viruses.

Certain viruses can become localized in neoplastic tissue and cause cell necrosis. Unfortunately, the tumour develops an immunity after an interval and shows signs of regrowth. Egypt 101 virus has been used for this purpose, after its tendency to induce encephalitis has been decreased by repeated passage through embryonic tissues. In a proportion of cases of advanced cancer definite tumour regression was shown; but regrowth of the tumour occurred when immunity to the virus was established.

Radioactive Gold.

Radioactive gold is useful in the treatment of pleural or peritoneal effusions due to widespread carcinomatosis. The colloidal gold particles are rapidly removed from the serous fluid and deposited on the walls of the serous cavity. Microscopic examination of the surface of the malignant nodules reveals superficial radiation damage and fibrosis, but similar changes are also seen in the general serous lining. Some of the radioactive gold is carried to the draining glands (this being beneficial, especially in the case of reticulosis), and some enters the blood-stream. There is, therefore, a temporary depression of the bone marrow after repeated treatment. The recommended dosage is 50 to 100 millicuries injected at monthly intervals, and this often results in decrease in size and rate of accumulation of the fluid.

Radioactive Iodine.

Radioactive iodine has been used in the treatment of advanced thyroid carcinoma. When it is administered orally, part of it is absorbed into secreting thyroid gland tissue, part is excreted in the urine, and the residue gives rise to whole body irradiation. For the treatment of thyroid carcinoma, a high pick-up by the tumour tissue is essential in order that the local radiation effects may be maximal. Unfortunately, only well-differentiated adenocarcinoma with colloid formation will pick up the isotope in high proportion, and thus only about 10% of all cases of thyroid carcinoma are suitable. This pick-up may be assisted by removing normal thyroid tissue by operation. In cases in which pick-up is high, there may be noted swelling and tenderness of the thyroid metastases after twenty-four hours, and relief of pain from bone metastases may be seen after a few days. Dosage levels are necessarily high, between 50 and 150 millicuries, the latter dose inducing a 25% fall in the level of the circulating white blood cells.

"Aureomycin."

It has been noted that "Aureomycin" is cytotoxic to tumour cells in tissue culture, and retards the growth of tumour grafts in mice. Therefore, it has been used as a synergist to nitrogen mustard in the treatment of advanced malignant disease. The intraarterial dosage is two milligrammes of nitrogen mustard and 500 milligrammes of buffered "Aureomycin" solution every eight hours for one to two weeks. Good results have been reported in a proportion of cases.

"Aureomycin" has also been combined with ACTH therapy in the treatment of advanced malignant disease, at a dosage of 500 milligrammes of the former and 10 units of the latter, at eight-hourly intervals, for five days. Good results were at first reported, but not confirmed by later workers.

Hormone Therapy.

The sex hormones have been freely used in the treatment of cancer, since Huggins introduced the use of œstrogens in the treatment of prostatic cancer. These hormones have the advantage of not being damaging (unlike some of the other remedies used in cancer), so that even if they are of no value they will do no great harm to the patient. An important difference in their mode of action from that of other methods of cancer treatment is that the aim is to modify the internal environment of the host and so increase the resistance of the patient to his tumour.

The development of the treatment of breast cancer by hormones was an outcome of Huggins's work on the prostate, and bore little relation at first to the hormonal control of the breast. In the case of the prostate, the hormonal control is relatively simple. The organ is acted upon only by œstrogens and androgens; the effect of these hormones is not mediated via the pituitary or adrenal glands, and will therefore occur also in hypophysectomized or adrenalectomized animals. However, in an analysis of the hormonal control of breast development and secretion, the hormones involved include œstrogens, androgens, progesterone, and pituitary, adreno-cortical and thyroid hormones.

Prostatic Cancer.

In 1941 Huggins demonstrated that the high acid phosphatase values in prostatic carcinoma could be reduced by bilateral orchidectomy or by œstrogen administration. Histological changes in the malignant cells following the use of œstrogens include disappearance of the mitotic figures and vacuolation of the cytoplasm. Clinical changes include decrease in the size of the primary growth within one to four weeks, regression of glandular, lung and bone metastases, relief of urinary obstructive symptoms, gain in weight, and disappearance of pain from metastases in one to two weeks. However, side effects include gynæcomastia, impotence and azoospermia, all the changes being reversible on stopping the drug. Less than 10% of patients fail to respond clinically, these patients being mainly those suffering from anaplastic carcinoma.

The dosage is one to five milligrammes of stilbœstrol three times a day, and the spread of the neoplasm can be inhibited by this means for two to three years in most cases and up to ten years in some cases. Surgical castration may be added if regression of growth is not pronounced, and adrenalectomy may give further prolongation of life.

Breast Cancer.

Œstrogens have been found of value in the treatment of advanced breast cancer, particularly in the post-menopausal age groups. Regression of the primary growth and of soft-tissue metastases is noted in approximately 60% of patients aged above sixty years, and even lung metastases may be controlled for periods of one to two years. Relief of pain

from bone metastases is less commonly seen. Administration of the drug for two to three months is usually necessary before definite regression can be noted.

Side effects include nausea or vomiting, uterine bleeding (of the œstrogen withdrawal type usually), and pigmentation of the nipples. In pre-menopausal cases there is definite evidence of increase of neoplastic activity following the administration of œstrogen, and its use is therefore contraindicated in these cases.

The dosage prescribed is 0·5 to 5·0 milligrammes of stilbœstrol three times a day, but 0·025 to 0·25 milligramme three times a day of the less toxic compound ethinyl œstradiol may be used.

Androgens are used in breast carcinoma on analogy with the use of œstrogens in prostatic carcinoma. It is likely that their action is by suppression of the pituitary gonadotrophic hormone or by creation of a hormonal imbalance. They are useful in the relief of pain from multiple bone metastases in breast carcinoma, and occasionally may control the growth of soft-tissue metastases. Relief is limited to a period of one to two years usually. They are thus indicated in all pre-menopausal cases of disseminate disease, and also when œstrogens fail in the post-menopausal cases.

Equivalent dosage levels are as follows: 400 milligrammes monthly by implantation; 800 milligrammes monthly by intramuscular injection; 1600 milligrammes monthly by oral "Linguets".

Relief of pain takes four to eight weeks to show itself, and control of soft-tissue growth about two to three months.

Side effects include masculinization (hirsuties, amenorrhœa and hoarseness), acneiform rashes and seborrhœa. There follow increase of energy and libido, and a tendency to gain in weight (associated with fluid and nitrogen retention). A rise in the blood urea level and a fall in the serum calcium level must be watched for.

Conclusion.

It is thus obvious that the door has been opened, perhaps not too widely at present, to a new agent in the treatment of cancer. It is possible that within the next ten or twenty years our present relatively crude methods of treatment will be replaced by the selective biological effects of chemotherapy in cancer of all types.

Reports of Cases.

TREATMENT OF NEPHROSIS WITH "SALT POOR" CONCENTRATED SERUM ALBUMIN (HUMAN).

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WITH the advent in this country of concentrated serum albumin in adequate supply for therapeutic purposes, it is thought that there are others who may be interested in the following account of its use in a case of nephrosis.

Clinical Record.

On May 25, 1954, the patient, a twenty-eight-years-old married woman, presented herself at the Mater Misericordiæ Hospital, Brisbane, with a history of intermittent ascites and peripheral œdema over the preceding five years. Both ascites and œdema had been present constantly for three weeks prior to her admission to hospital.

On examination of the patient, significant findings were as follows. The patient was pale, had severe sacral, leg and ankle œdema, and had definite ascites. Her blood pressure was 160 millimetres of mercury, systolic, and 100 millimetres, diastolic. Laboratory investigations showed a blood urea content of 30 milligrammes per 100 millilitres of blood and a serum cholesterol content of 365 milligrammes per 100 millilitres of serum. The ward urine test showed a deposit of protein about three-quarters of the volume of urine tested. Microscopic examination of the urine revealed a few hyaline casts and an occasional leucocyte and red cell per high power field. The urine on attempted culture was found to be sterile.

The patient was treated with a high protein and low salt diet for five weeks with no significant improvement in her clinical state or the laboratory findings. It was then decided to attempt to obtain diuresis by the use of dextran given intravenously. However, after the administration of only 120 millilitres in the first transfusion with "Dextraven" (dextran, Benger) 6% in saline, the patient developed an acute allergic reaction—intense pruritus, urticarial weals, projectile vomiting and headache—necessitating immediate cessation of this form of therapy.

Over the succeeding four weeks, with the patient receiving a high protein low salt diet only, her clinical state deteriorated. Her ascites became so severe as to necessitate *paracentesis abdominis*, which, with the removal of 35 ounces of fluid, effected only very temporary improvement.

It was then decided to attempt to obtain diuresis by the use of "salt poor" albumin (normal serum albumin (human) as prepared by the Commonwealth Serum Laboratories, Melbourne, each unit containing 25 grammes of human albumin in 100 millilitres of solution buffered with acetyl tryptophane). Each unit was administered within half to one and a half hours. Two courses of albumin therapy were given. The patient received a first course of 23 units of albumin in twenty-six days, followed by an intermission of ten days, in which no albumin was given, and then a further course of 10 units in eleven days.

The patient had diuresis on the tenth day of treatment, and this persisted for the remainder of the time she was under observation. Besides albumin, the patient was given blood or red cell concentrate (R.C.C.), according to the daily hæmoglobin estimation. Sodium bicarbonate and potassium citrate were exhibited for correction of acidosis and electrolyte drifts.

Prior to the commencement of therapy with albumin, the serum protein content was 3·7 grammes (albumin 1·8 grammes, globulin 1·85 grammes) per 100 millilitres of blood; the blood urea content was 56 milligrammes per 100 millilitres of blood.

Table I is a record of the patient's response to therapy during the two successive courses of treatment which commenced on August 9, 1954.

The patient was discharged from hospital relieved of all signs and symptoms, and has been maintained in a satisfactory state up to the time of writing (two months after date of discharge from hospital), although her serum protein value is now 4·9 grammes per 100 millilitres of blood, her hæmoglobin value is 13·8 grammes per 100 millilitres of blood, and her carbon dioxide combining power (despite large doses of sodium bicarbonate and potassium citrate) is only 54 volumes per 100 millilitres of plasma. However, there has been no recurrence of œdema.

Discussion.

1. During the first course of albumin therapy, there were two marked phases. The first—generally attributed to an expansion of blood volume—was associated with the symptoms of acute hypertension and was confirmed by the blood pressure findings as shown above. The fall in serum protein levels over this period would appear to lend support to this view. The second phase was characterized by onset of diuresis, reduction of anasarca and removal of symptoms of hypertension.

2. The second course of albumin therapy was initiated because of a recurrence of the rise in the patient's weight, which was taken to represent a reaccumulation of fluid in tissues.

3. Paper electrophoretic analysis was carried out on samples of the patient's serum before and during treatment. The initial pattern indicated decreased serum protein

TABLE I.[1]

Day.	Therapy.	Blood Pressure. (Millimetres of Mercury.)	Weight. (Pounds.)	Urinary Output. (Ounces per 24 Hours.)	Urine Ward Test. (Deposit: Proportion of Sample.)	Hæmoglobin Value. (Grammes per 100 Millilitres.)	Blood Urea Content. (Milligrammes per 100 Millilitres.)	Serum Sodium Content. (Milliequivalents per Litre.)	Serum Potassium Content. (Milliequivalents per Litre.)	Plasma Carbon Dioxide Combining Power. (Volumes per 100 Millilitres.)	Serum Protein Content. (Grammes per 100 Millilitres.)	Remarks.
1	100 millilitres R.C.C. 1·0 unit albumin.	—	—	40	1/8	3·6	56	—	—	—	—	
2	500 millilitres R.C.C.	140/90	—	35	1/10	6·5	—	139	4·6	52	4·3	
3	300 millilitres R.C.C. 500 millilitres blood.	—	—	35	1/20	7·9	69	—	—	—	—	
4	0·5 unit albumin ..	150/105	138	31	1/10	10·0	53	143	4·7	60	4·3	Technical difficulty in transfusion.
5	230 millilitres R.C.C. 1·0 unit albumin.	—	141	22	3/4	8·9	64	—	—	—	4·2	
6	500 millilitres R.C.C. 1·0 unit albumin.	—	141	35	3/4	10·9	54	—	—	—	4·2	
7	500 millilitres blood.	—	141	27	Solid	12·3	60	—	—	—	4·2	Headache.
8	1·0 unit albumin ..	170/100	146	42	1/2	12·1	58	—	—	—	3·9	Headache.
9	1·0 unit albumin ..	170/130	143	35	1/2	12·3	57	—	—	—	3·5	Headache and nausea.
10	1·0 unit albumin ..	180/120	138	66	1/3	12·3	55	—	—	—	—	Headache.
11	1·0 unit albumin ..	190/120	133	95	1/3	11·6	48	147	4·8	50	4·4	
12	1·0 unit albumin ..	190/120	133	93	1/3	10·0	45	156	4·7	64	4·7	
13	300 millilitres R.C.C. 1·0 unit albumin.	170/115	130	101	1/2	10·0	48	148	4·5	68	—	
14	1·0 unit albumin ..	180/120	129	107	1/3	11·6	49	152	4·5	69	4·4	
15	1·0 unit albumin ..	190/120	126	73	—	11·6	64	150	4·5	66	4·6	
16	1·0 unit albumin ..	180/120	—	104	1/6	11·6	52	148	4·5	66	4·5	
17	1·0 unit albumin ..	200/125	—	58	1/2	11·4	58	150	4·0	60	4·0	
18	1·0 unit albumin ..	175/105	—	74	Solid	11·4	48	137	4·1	66	4·1	
19	500 millilitres R.C.C. 1·0 unit albumin.	175/110	—	84	Solid	10·9	45	145	4·7	62	4·6	Œdema absent.
20	1·0 unit albumin ..	160/100	116	83	1/2	12·3	46	147	4·3	64	4·7	
21	1·0 unit albumin ..	170/100	115	72	1/3	11·9	46	147	4·2	63	4·8	
22	1·0 unit albumin ..	160/110	111	53	3/4	11·9	60	143	4·3	60	5·2	
23	1·0 unit albumin ..	170/100	111	56	7/8	11·6	90	143	4·7	62	5·0	
24	1·0 unit albumin ..	170/100	113	52	3/4	11·6	87	145	4·6	64	5·2	Hess's test: positive result.[2]
25	1·0 unit albumin ..	170/100	112	48	Solid	11·6	79	145	4·3	62	5·2	
26	400 millilitres blood 1·0 unit albumin.	160/105	111	63	1/3	10·9	67	—	—	64	5·2	
27	Nil	170/105	111	53	1/2	11·6	75	—	—	62	5·2	
28	Nil	195/120	112	57	1/12	—	70	—	—	—	5·3	
29	Nil	165/110	112	63	1/3	11·6	72	—	—	62	5·2	
30	Nil	185/120	113	60	1/3	11·6	73	—	—	—	5·2	
31	Nil	190/125	114	39	1/6	11·6	69	—	—	—	5·4	
32	Nil	190/120	113	32	1/4	11·9	—	—	—	—	—	
33	Nil	180/115	113	37	1/2	11·2	54	—	—	—	5·3	
34	Nil	190/125	115	55	1/4	11·6	52	—	—	—	5·3	
35	Nil	160/105	116	73	1/2	—	—	—	—	—	—	
36	Nil	160/105	118	48	1/6	11·6	57	—	—	58	4·4	
37	1·0 unit albumin ..	160/105	114	79	1/6	11·6	66	—	—	58	4·9	
38	1·0 unit albumin ..	160/110	114	47	—	11·6	52	—	—	60	4·6	
39	1·0 unit albumin ..	160/110	114	83	1/3	11·9	60	—	—	52	4·7	
40	1·0 unit albumin ..	165/115	115	51	1/24	8·9	65	—	—	64	5·2	
41	300 millilitres R.C.C.	165/100	117	82	—	9·4	55	—	—	66	4·8	
42	Nil	—	118	59	1/2	—	—	—	—	—	—	
43	500 millilitres blood	165/115	120	71	1/10	11·4	52	—	—	66	4·5	
44	500 millilitres blood	155/110	122	88	1/6	12·3	57	—	—	70	4·8	
45	1·0 unit albumin ..	165/110	122	79	1/8	12·9	—	—	—	—	—	
46	1·0 unit albumin ..	155/110	122	106	1/20	12·4	61	—	—	74	4·8	
47	2·0 units albumin	165/110	120	104	Trace	12·4	55	—	—	68	4·7	
48	1½ units albumin	—	119	50	1/3	11·6	55	—	—	62	4·7	
49	Nil	—	119	52	1/4	—	—	—	—	—	—	
50	400 millilitres blood	160/110	119	85	—	11·6	84	—	—	68	5·2	
51	500 millilitres blood	175/120	119	72	1/3	—	76	—	—	66	5·5	Hess's test: negative result.
52	Nil	—	120	64	1/3	12·9	79	—	—	66	5·3	
53	Nil	170/110	120	—	1/2	12·9	79	—	—	66	5·2	

[1] The patient had two courses of procaine penicillin, 400,000 units twice a day, during the courses of therapy—namely from August 16 to 18, 1954, and from September 19 to 23, 1954. In each case the indication was pyrexia.

[2] No reason was found in the positive result in Hess's test. The result of this test was noticed to be positive on September 1, 1954 (that is, the twenty-fourth day) and remained definitely positive until September 28, 1954, though not nearly so marked as when first noticed four weeks earlier. Investigations carried out revealed no obvious cause—platelets were normal, red cell fragility was normal, prothrombin time and findings from other investigations were within normal limits.

content, with a marked decrease in the albumin fraction. After treatment, whilst the albumin concentration had returned almost to normal, the concentration of all the globulins had increased, although the total serum protein content was still less than normal. It is of some interest to note that restoration of all fractions of serum protein occurred during the courses of treatment. Although it is tempting to suggest that the albumin therapy provided essential amino acids from which other protein fractions could be synthesized, it is just as possible that improvement in gut function consequent upon the reduction in anasarca (with the onset of diuresis) resulted in better absorption of protein from the diet. There was no significant change in dietary treatment of this patient during her stay in hospital.

4. It is of interest to note that although a unit of albumin was given within half to one and a half hours, there was no significant alteration in urinary electrophoretic pattern at one and four hours after commencement of albumin transfusion. The urinary electrophoretic patterns indicated that the protein consisted mainly of albumin, but there were traces of all the globulins. However, there was no significant increase in excretion of albumin, which would have been shown by a rise of the albumin fraction of the later electrophoretic pattern.

Acknowledgements.

I wish to thank Dr. A. J. Morton for permission to report this case. I am indebted to the Sisters of Mercy for permission to publish the findings. I am also indebted to Dr. A. E. Shaw of the Red Cross Blood Transfusion Service (Queensland) for help and supervision of the courses of albumin therapy, and to Mr. J. E. O'Hagan, biochemist of the above Service, for conduct and interpretation of electrophoretic analysis as well as for checks, by Kjeldahl estimation, of certain of the serum protein findings.

FATAL BITE FROM OCTOPUS.

By H. FLECKER,
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AND
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Adelaide.

As no similar tragedy can be discovered in the medical or other scientific literature, the following incident is worth recording in detail. We are much indebted to Dr. J. V. Quinn, Medical Superintendent of the Darwin Hospital, at Darwin, Northern Territory, for clinical details.

Clinical Record.

A., an able-bodied seaman, aged twenty-one years, a member of the Arafura Skin Divers' Club, on October 19, 1954, had been fishing with a comrade, B., during the afternoon off East Point Beach, three miles from the township, just inside the eastern head of the Darwin Harbour, when the latter noticed a small blue octopus about six inches long swimming in the water beside them. As they were leaving the water, B. put the octopus on his shoulder and walked ashore for some distance with the animal on his body. When they reached shallow water, he called to A. to see whether he wanted the octopus. A. replied in the affirmative, the octopus was thrown to him, lodging on his shoulder, and he walked ashore to the beach. As they were about to leave the water, A. said that they did not want the octopus any more, and it was thrown back into the sea. Shortly afterwards, he began to complain of dryness in the mouth, followed by difficulty in breathing. No complaint of sting or pain of any kind was made, although a small bleeding puncture was noted at the site where the octopus was placed. A. refused an offer to be taken to a doctor at this time, but his condition grew progressively worse, and later he complained that he could not swallow, became nauseated and then started to vomit. He was placed in a car and rushed to the Darwin Hospital, a distance of some four miles. On arrival, he was found to be cyanosed and not breathing, although his heart was still beating. Emergency treatment, including the giving of adrenaline and "Anacardone" and the use of a respirator, produced no effect, and the heart stopped beating about a quarter of an hour after his admission to hospital. Both the doctor on duty and A.'s companion noticed at the time of his admission to hospital that there was a small reddish mark on the right shoulder where the octopus had lodged, but this faded rapidly.

An autopsy was held, but no organic disease was found. The mark on the shoulder had faded and could not be found.

Other facts worth recording are that the victim was known to have asthma of mild degree, and that both he and his companion were experienced spear fishermen and accustomed to the various sea animals. Although his symptoms are not typical of allergic response, the possibility of some hypersensitivity reaction exists.

Later on, B. brought in an octopus, which he stated was identical in every respect, including size, with the one with which they were "skylarking". What was now dull blue was an iridescent blue when the animal was first produced. However, the ability of the live octopus to change its colour according to the nature of its environment is well known.

Comment.

The specimen proved to be *Octopus rugosus* Bosc, 1792 (*Actes Soc. hist. nat. Paris*, 1: 24, plate 5, figures 1, 2). It is of cosmopolitan distribution, being found in the seas around New South Wales, Queensland, Northern Australia, Port Essington, Thursday Island, Torres Strait and now Darwin. Synonyms are numerous, *O. granulatum* Lamarck, *O. americanum* Montfort, *O. tuberculatum* Blainville *et cetera*. Some even state that it is a form of the large common Japanese *O. vulgaris*, which is known to be poisonous; but neither that species nor, for that matter, any giant octopus, has been definitely recorded from off the Australian coast, although *O. vulgaris* occurs in the East Indies.

O. rugosus is a shallow-water species found in the littoral zone among corals and rocks. The eggs, over which it broods, are usually attached to rocks and frequently to the inside of dead shells. The general anatomy is similar to that of *O. vulgaris*. R. Krause in 1895 demonstrated the existence of anterior and posterior "salivary" glands. In 1905 Briot studied the venom of cephalopods. Rouville in 1910 studied the toxicity of glandular extracts in mammals. Despite the fact that from earliest times the octopus has been used as food in various countries, both in Europe and in Asia, there is no record of human bites until that of Halstead in 1949, except probably that of Denys Montfort in 1802. He gives an interesting and humorous description of an encounter between a dog and octopus at Havre, adding that he was painfully bitten on the right hand.

As recently as 1954 four cases of bites to human hands have been recorded in California by Berry, who gives the following summary:

> Symptoms consisted of a sharp pain upon contact (described as similar to a bee sting), tingling, throbbing, redness, swelling, and in one case abnormally profuse bleeding. Symptoms seem to vary considerably, depending upon the size and possibly the species of octopus, the site of the wound, and doubtless the amount of venom injected. Octopus bites are of the puncture wound variety and with the smaller animals commonly handled are relatively minor in nature. Little is yet known regarding the pharmacological and biochemical properties of the toxin.

The species concerned are mentioned as being probably *Octopus rubescens* Berry, *Octopus fitchi* and *Octopus* (*Paroctopus*) *appollyon* Berry.

There is a tremendous gap between the relatively trivial cases which have been described and that which ended fatally at Darwin.

G. E. MacGinitie, director of the Kerckhoff Marine Laboratory, California, described how *Octopus appollyon* held a crab with the web and tentacles and sprayed the victim with venom. "The crab was not touched by the beak of the Octopus until it (the crab) had been dead twenty minutes."

There may be four or five so-called "salivary glands" in the octopus, two anterior, one sublingual and two posterior. However, the "salivary glands" do not secrete digestive enzymes, but a poison used in capturing their prey. Both anterior and posterior pairs produce a toxin, but the principal source of the more virulent poison is the posterior pair.

The venom is used by the octopus to kill crabs, molluscs and fish, including sharks. When poison removed from the posterior salivary glands of *Octopus vulgaris* was injected into the shore crab, *Carcinus mænus*, the crustacean "developed a type of locomotor ataxia which was followed by a series of rapid tremors, convulsive movements, and then death, the entire episode lasting only a very few minutes".

Many suggestions have been made as to the nature of the poison, but Bertil Hanstrom (1939) writes as follows

of cephalopods: "Tyramin is a normal product of the posterior salivary gland (poison gland) and is not only found in the saliva but also in the blood." The compound tyramin is produced from the decarboxylation of tyrosine.

Tyramin contracts the chromatophore muscles and thus expands the chromatophores or "colour spots", darkening the skin surface of the octopus during colour changes. Betain, also found in the muscles of the octopus, acts antagonistically to tyramin and contracts the chromatophores, thereby making the skin lighter.

When the octopus eats, it becomes darker through the stimulation of the salivary glands, while the animal is paler when hungry.

FIGURE I.

Presence or Absence of Salivary Glands in the Cephalopoda (Phylum Mollusca).

There are two subclasses of the Cephalopoda—the Tetrabranchiata, with two pairs of gills, and the Dibranchiata, with one pair of gills. The former is represented by one family, Nautilidæ, one genus, *Nautilus*, and six species in which anterior salivary glands are present, the posterior absent.

The subclass Dibranchiata is divided into two orders, Octobrachiata with eight arms and Decembrachiata with ten.

Order Decembrachiata has two suborders. Myopsida have the eyes covered with an imperforate membrane, and are mostly sublittoral species; the following are examples: *Sepia* (cuttlefish with calcified internal shell); *Loligo*, *Sepioteuthis* (squid with chitinous internal shell), with slightly developed anterior salivary glands represented by an unpaired intrabulbular mass and posterior salivary glands. Oegopsida have the eye-covering membrane perforate over the cornea, and are mostly pelagic species. Examples are the *Spirula* (with internal post horn shell), *Architeuthis* (giant squid), *Onychoteuthis* (claw squid), with large anterior salivary glands and posterior also present.

Order Octobrachiata, which includes the species of typical *Octopus*, contains two suborders.

Suborder Cirrata covers those octopus-like species with fins. There are two superfamilies Vampryoteuthacea and Cirroteuthacea. In the first there is as yet no record of the presence or absence of either anterior or posterior salivary glands. In the second the anterior salivary glands are very small, the posterior absent.

Suborder Incirrata is divided into three superfamilies, Bolitænacea, Octopodacea and Argonautacea. The first superfamily is represented in Australia by *Eledonella sheardi* Allan, 1945 (New South Wales), of the family Bolitænidae, and *Amphitretus pelagicus* Hoyle, 1885 (Tasmania), of the family Amphitretidae. In these the pair of anterior glands are present and also larger posterior glands, as is the case with the Octopodacea, containing the typical Octopodidæ. The Argonautacea, example *Argonauta nodosa* (Paper Nautilus), have anterior and smaller posterior salivary glands.

Species of octopus recorded from Australia are set out below.

Octopus vulgaris Lamarck, 1798, subfamily Octopodinæ (*Bull. Soc. phil. Paris*, 2: 130). This rough-skinned, rich yellow-brown species, growing up to five feet in length, is common in deeper waters around Japan, Indo-Pacific coasts and America, and in all probability occurs off our northern coasts. It is known to be poisonous.

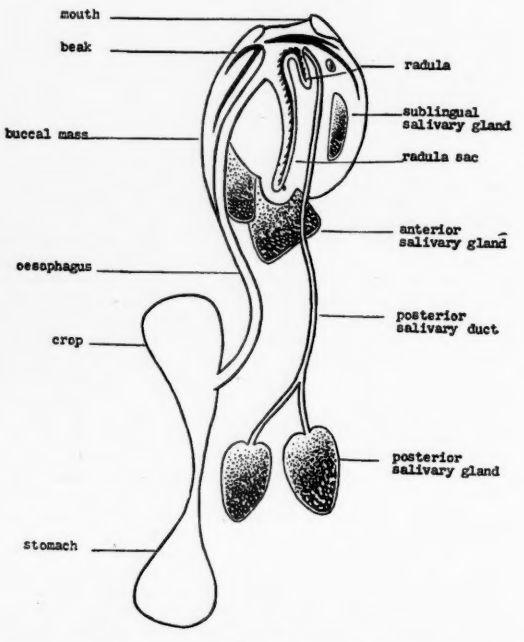

FIGURE II.

Octopus rugosus Bosc, 1792; *Sepia* (*Actes Soc. nat. Paris*, 1: 24). This species is distinguished by the purplish ground colour and lighter reddish colour of the ventral body and inside surface of the arms. The skin is granular, with a wart-like texture. It may be six to fifteen inches in length when fully grown, and is common in littoral shallow waters of rock and coral reefs. It has been recorded from Port Essington, Thursday Island, Torres Strait, Queensland and New South Wales, and Dr. C. M. Deland describes it as common on New Guinea reefs. The specimen forwarded from Darwin by Dr. Quinn was a female of this species, and is said to be similar to the one which caused the fatality.

Octopus tenebricus Smith, 1884 (*Zool. "Alert" Moll.*, page 35, plate 4, figures B-B3). This species is dark purplish chocolate in colour and about three inches long. Queensland Port Denison (type).

Octopus duplex Hoyle, 1885 (*Ann. Mag. Nat. Hist.*, (5) 15: 222). This species has a weakly granular skin surface and is about four inches long. It is found off New South Wales, Tasmania and Victoria.

Octopus cyanea Gray, 1849 (*Cat. Moll. Brit. Mus.*, (1), page 15). This species is smooth, reddish, maculated with purple,

and two feet long. It is found in shallow water off New South Wales and Queensland.

Octopus tetricus Gould, 1852 (*Moll. Wilkes Exped.*, page 474, figure 588). The skin surface is covered with rosette-like tubercles. The octopus is 18 inches long. It is found off New South Wales.

Octopus macropus Risso, 1826 (*Hist. Nat. Eur. Merid.*, 4: 3). This species is reddish-brown and the skin has a granular surface. This octopus is five feet long. It is found off New South Wales.

Octopus membranaceus Quoy and Gaimard, 1832 (*Voy. "Astrolabe", Zool.*, 2: 89, plate 6, figure 5). This species has ocular and cephalic cirrhi, and the skin surface is granular. The octopus is three inches long. It is found off New South Wales, in Bass Strait, off Tasmania, and off Western Australia.

Octopus flindersi Cotton, 1932 (*Rec. South Australian Mus.*, (4) 4: 543, figures 4, 6). This species is reddish-brown, maculated with darker brown spots; the ventral surface and inner surface of the arms are yellowish. It may grow up to eight feet in length. It is found off South Australia. It usually lives in deeper waters, but is sometimes found in shallow waters.

Octopus pallida Hoyle, 1885 (*Ann. Mag. Nat. Hist.*, (5) 15: 22). This species is pale purplish-grey, shading to creamy-white on the ventral surface. The skin is completely covered with neat rosette-like tubercles. The octopus is 12 inches long. It is found off New South Wales, South Australia, Western Australia and Victoria, on reefs and down to 200 fathoms.

Octopus australis Hoyle, 1885 (*Ann. Mag. Nat. Hist.*, (5) 15: 224). This species is yellowish, mottled and spotted with light or dark brown. The skin surface is granular. The octopus is six inches long. It is found off New South Wales, Victoria, South Australia and Western Australia.

Octopus superciliosus Quoy and Gaimard, 1832 (*Voy. "Astrolabe", Zool.*, 2: 88, plate 6, figure 4). This species is whitish, the skin surface is granular. The length is four inches. It is found off Victoria.

Octopus cærulescens Blainville, 1826 (*Dict. Sc. Nat.*, 42: 129). This octopus is blue, and it is two and a half inches long. It is found off Australia.

Octopus peroni d'Orbigny, 1826 (*Ann. Sc. Nat.*, (1) 7: 144). This species is found in the waters round Australia.

Tritaxeopus cornutus Owen, 1881 (*Tr. Zool. Soc. London*, (5), 51: 131, plate 23). The skin surface has sparse warts, the eyelids are heavily caruncluated and bear large cirrhi, hence the name. The species is two feet long. It is found in the waters round Australia.

Hapalochlæna lunulata Quoy and Gaimard, 1832. *Octopus* (*Voy. "Astrolabe", Zool.*, 2: 86, plate 6, figure 1). This species has a colour pattern of iridescent blue rings. The skin is smooth and gelatinous. The octopus is six inches long. It is found off Western Australia, New South Wales and northern Australia.

Hapalochlæna maculosa Hoyle, 1883. *Octopus* (*Proc. Phys. Soc. Edinburgh*, 8: 319, plate 6). This is yellowish with darker maculations occupied by light blue iridescent, sometimes raised, rings. The octopus is four and a half inches long. It is found off Western Australia, South Australia, Tasmania, Victoria, New South Wales and Queensland. A littoral species is sometimes taken in 15 fathoms.

The following are examples of the subfamily Bathypolypodinæ:

Grimpella thaumastocheir Robson, 1928 (*Ann. Mag. Nat. Hist.*, (10) 11: 108, figures 1-4). This is purplish-brown, and the skin has widely spaced warts. The funnel organ is double and there is no ink sac. The posterior pair of salivary glands are very large. The radula is somewhat degenerate. This octopus is of the shallow-water, débris-eating type, and is six and a half inches long. It is found off South Australia (Port Lincoln). One specimen, a male, is the only one known.

Bathypolypus sp.? Hoyle, 1881 (*"Challenger" Zool.*, (44) 16: 101). Fragments were taken in 1400 fathoms east of Cape York.

Bentheledone rotunda Hoyle, 1885. *Eledone* (*Ann. Mag. Nat. Hist.*, (5) 15: 230). This is found in the Southern Ocean east of Kerguelen and south-west of Cape Leeuwin, Western Australia; it has been taken in 1950 fathoms.

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A COAGULATION DISORDER DUE TO A FACTOR VII-LIKE DEFECT.

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IT is generally recognized that the one-stage prothrombin test of Quick (1935) is dependent upon other factors in addition to prothrombin. Deficiencies of factor V (Owren, 1947), of factor VII (Koller, Loeliger and Duckert, 1951), or of fibrinogen, or the presence of excessive amounts of certain anticoagulants will cause prolongation of the one-stage prothrombin time. A deficiency of prothrombin alone is extremely rare (Biggs and Douglas, 1953), and in the majority of reported instances the diagnosis has been made on inadequate grounds.

Owen and Bollman (1948) described a factor in serum capable of correcting the coagulation defect in patients treated with dicoumarol. They called this substance "prothrombin conversion factor". De Vries, Alexander and Goldstein (1949) also described the same substance and named it "serum prothrombin conversion accelerator (S.P.C.A.)". Owren (1950, 1951, 1952*a*) called this serum factor "convertin", and demonstrated that it was formed during coagulation from a precursor which he named "proconvertin". Koller, Loeliger and Duckert (1951, 1952) showed this substance to be an accelerator of prothrombin conversion and named it "factor VII".

Factor VII is also required for the formation of thromboplastin. Jacox (1949) has shown that the addition of serum enhances the thromboplastic activity of brain emulsion. Biggs and Douglas (1953*b*) have shown that if the serum from patients treated with "Tromexan" is used in the thromboplastin generation test, the generation of thromboplastin is reduced parallel with the reduction of factor VII.

Several instances of probable factor VII deficiency have been described in the literature (Alexander, Goldstein,

Landwehr and Cook, 1951; Owren, 1952; Beaumont and Bernard, 1953; Marciniakowna, Krakowska, Bober and Safarzynska, 1953; Jenkins, 1954*a*). A further similar case was published by Crockett, Shotten, Craddock and Leavell (1949) as "Ac globulin deficiency", and Giordano (1943) described another, but called it "hypoprothrombinæmia". Still other cases published as idiopathic hypoprothrombinæmia could well have been due to factor VII deficiency. One of these (Hagen and Watson, 1948) has since been restudied and published again as a "congenital familial deficiency of the stable prothrombin conversion factor" (Frick and Hagen, 1953).

Clinical Record.

The patient was a girl, aged sixteen years. When she was a baby it was noted that eruption of her teeth was always preceded for several days by the appearance of a vesicle filled with blood. Later, when she lost these first teeth, her gums would ooze for one or two days. At twenty-one months and again at twenty-seven months she underwent operations for repair of umbilical hernia, and no abnormal bleeding was recorded. When she was aged five years she had a severe epistaxis, and eight months later she had three more epistaxes in six weeks. She has had occasional epistaxes since that time. An appendicectomy was performed when she was eight years old, and apparently the wound bled when the clips were removed. Some teeth were extracted when she was aged eleven years, and she spent the following five days in hospital waiting for the bleeding to stop. Fifteen months later more teeth were removed, and although the cavities were packed with "Oxycel" gauze, they oozed for over a week and blood transfusion was required.

The menarche occurred at the age of eleven years, and her first menstrual period lasted for two weeks. Three months later the next menstrual period commenced, and on this occasion the bleeding was so severe that a transfusion of one and a half litres of blood was given. Since then her menstrual periods have always been excessive, and they last on an average for twelve days. Recently she underwent a diagnostic curettage. A severe hæmorrhage followed, which was controlled by blood transfusion.

Over the last four years she has received seven transfusions, in which a total of about ten litres of blood has been given. On each occasion blood transfusion has promptly controlled the bleeding. Injections of vitamin *K* and vitamin K_1 produced no improvement, either clinically or in the coagulation mechanism.

No other members of the family have shown any bleeding tendencies.

Investigations.

The hæmoglobin value was 12·8 grammes per 100 millilitres, the leucocyte count was 4200 per cubic millimetre, and the blood film appeared normal. After the hæmorrhage resulting from the diagnostic curettage the hæmoglobin value fell to 4·6 grammes per 100 millilitres. The bleeding time (Ivy's method) was two minutes. The whole blood clotting time (modified method of Lee and White, 1913) was six minutes (normal, five to ten minutes). The recalcified plasma clotting time was 100 seconds (normal, 90 to 250 seconds).

The one-stage prothrombin test (Quick, 1935) was carried out with both rabbit and human brain as sources of thromboplastin. A 5% suspension of the acetone-treated material was prepared. Russell's viper venom ("Stipven"—Burroughs Wellcome) was used alone and also together with lecithin. The results of these tests are shown in Table I. A pronounced abnormality was demonstrated with brain extracts, but not with Russell's viper venom.

The effect of different substances on the abnormality in the patient's one-stage prothrombin time is shown in Table II. Normal plasma and normal serum corrected the defect. "Dindevan" plasma and aluminium hydroxide-treated plasma improved it, but did not correct it. Addition of the patient's own serum was ineffective.

Serum was found to have a greater ability to correct the defect than plasma, as is shown in Table III. The addition of 6·25% of serum was sufficient to bring the prothrombin time to within one second of normal. Factor VII is more active in serum than in plasma. Owren (1950, 1951, 1952*a*) named the serum substance "convertin" and the plasma precursor "proconvertin".

The effects on the one-stage prothrombin time of adding 20% of normal serum and 20% of patient's serum to the plasma of patients on "Dindevan" therapy are compared in Table IV. The patient's serum improved the prothrombin times, but not so much as did normal serum.

TABLE I.

One-Stage Prothrombin Test with Different Thromboplastin Preparations.

Thromboplastin Preparation.	Patient's Plasma Prothrombin Time. (Seconds.)	Normal Plasma Prothrombin Time. (Seconds.)
Rabbit brain	28 to 105[1]	11·5 to 14[1]
Human brain	45	13
Russell's viper venom (" Stipven ")	10	17
Russell's viper venom with lecithin	6	6

[1] The limits of the range of results obtained from estimations on six different occasions.

TABLE II.

The Effect of Different Substances on the Patient's One-Stage Prothrombin Time (Rabbit Brain Thromboplastin).

Test Material.						One-Stage Prothrombin Time in Seconds.
Patient's Plasma.	Normal Plasma.	Normal Serum.	" Dindevan " Plasma.	Aluminium Hydroxide Treated Normal Plasma.	Patient's Serum.	
100%	—	—	—	—	—	105
—	100%	—	—	—	—	12
—	—	100%	—	—	—	No clot
—	—	—	100%	—	—	55
—	—	—	—	100%	—	500
50%	50%	—	—	—	—	12
50%	—	50%	—	—	—	12
50%	—	—	50%	—	—	39
50%	—	—	—	50%	—	37
50%	—	—	—	—	50%	No improvement[1]
—	—	50%	50%	—	—	13

[1] Done on a different day, and results not comparable.

Incubation at 37° C. for one hour of the patient's plasma and normal plasma with rabbit-brain preparation was carried out. The prolongation of the one-stage prothrombin time after this incubation was not significantly greater than that observed in the control.

TABLE IIIA.

One-Stage Prothrombin Times of Varying Mixtures of Patient's Plasma with Normal Plasma (Rabbit Brain Thromboplastin).

Patient's Plasma. (*Per Centum.*)	Normal Plasma. (*Per Centum.*)	Prothrombin Time. (Seconds.)
—	100·0	11·5
50·0	50·0	12·0
75·0	25·0	12·0
87·5	12·5	13·0
93·75	6·25	15·5
100·0	—	28·0

The thrombin generation test (Macfarlane and Biggs, 1953; Pitney and Dacie, 1953) was modified in the following way. Whole citrated blood, 0·5 millilitre, saline, 0·5 millilitre, and M/40 calcium chloride solution, 0·5 millilitre, were mixed together and incubated at 37° C. At intervals of

one minute 0·1 millilitre samples were taken in a graduated Pasteur pipette and blown into tubes containing 0·4 millilitre of fibrinogen preparation and the clotting times were noted. The clotting times were converted into units of thrombin by reference to a thrombin-fibrinogen curve prepared from dilutions of "Thrombin Topical" (Parke Davis). Aluminium hydroxide-treated plasma, to which had been added one-fourth volume of 2% pyrocatechol solution in "Veronal" buffer, was used as a source of fibrinogen. Pyrocatechol inhibits the action of antithrombins (Fantl, 1954), and gives faster clotting times and clearer end-points than preparations without antithrombin inhibitors. The generation of thrombin was within normal limits (Figure I).

TABLE IIIB.

One-Stage Prothrombin Times of Varying Mixtures of Patient's Plasma with Normal Serum (Rabbit Brain Thromboplastin).

Patient's Plasma. (*Per Centum.*)	Normal Serum. (*Per Centum.*)	Prothrombin Time. (Seconds.)
50·0	50·0	11·5
75·0	25·0	12·0
87·5	12·5	12·0
93·75	6·25	12·5
100·0	—	28·0

The two-stage prothrombin test (Biggs and Douglas, 1953*a*) was carried out with aluminium hydroxide-treated plasma to which had been added one-fourth volume of 2% pyrocatechol solution in "Veronal" buffer as a source of fibrinogen. The result, shown in Figure II, illustrates that there was no deficiency of prothrombin, since the areas enclosed by both curves were approximately equal. However, the curves obtained using the patient's plasma were flatter than that of the normal, with a delayed peak of thrombin generation indicating a slower than normal generation in this test.

TABLE IV.

The Effect of Adding 20% Normal Serum and 20% Patient's Serum respectively on the One-Stage Prothrombin Times of the Plasma of Patients Treated with "Dindevan".

Patient's Number.	One-Stage Prothrombin Times (Seconds).		
	"Dindevan" Plasma.	"Dindevan" Plasma *plus* 20% Patient's Serum.	"Dindevan" Plasma *plus* 20% Normal Serum.
1	22·0	17·0	15·0
2	32·5	24·5	19·0
3	47·5	41·5	17·0
4	32·0	27·0	20·5

By the prothrombin consumption test (Biggs and Macfarlane, 1953) a normal index of prothrombin consumption was obtained. It is possible that the abnormality in the patient's serum may have made these results not comparable with those of the control. The test was therefore repeated, normal serum being substituted for the saline used in this test. The results were again normal.

The thromboplastin generation test (Biggs and Douglas, 1953*b*) showed that thromboplastin was generated normally when the patient's platelets, aluminium hydroxide-treated plasma and serum were tested either separately or all together. As factor VII is known to be required for the formation of thromboplastin, it was thought that the normal results in this case could be due to the rapid interaction of the incubation mixture with factor VII supplied by the normal plasma substrate. For this reason the test was again performed with the use of the patient's own plasma as substrate. Normal results were again obtained, enough thromboplastin being generated after four minutes' incubation to clot the substrate plasma in eight seconds.

Discussion.

In the case presented the history suggests a congenital bleeding tendency which has progressed considerably during adolescence. Investigation of the coagulation mechanism showed a prolonged one-stage prothrombin time when brain extracts were used as a source of thromboplastin. The addition of small amounts of normal serum or plasma readily corrected this defect, which indicated that the patient was suffering from a deficiency state and not from the effects of a circulating anticoagulant. The deficiency, therefore, was of a serum factor which, like factor VII, is required for the conversion of prothrombin to thrombin by tissue extracts in the presence of calcium. The patient's plasma also resembled factor VII-deficient plasma in its reaction with Russell's viper venom in the

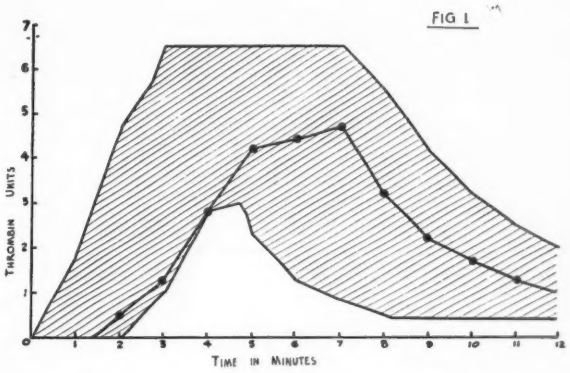

FIGURE I.

The thrombin generation test. The shaded area represents the limits of normal thrombin generation.

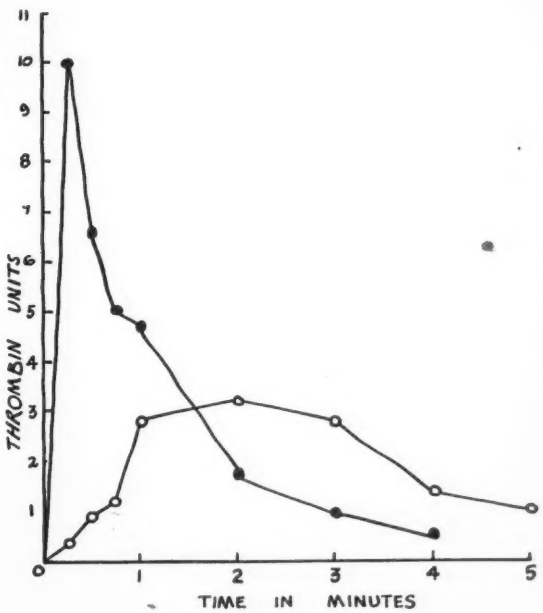

FIGURE II.

The two-stage prothrombin test. The test was carried out on normal plasma (solid circles) and on the patient's plasma (open circles).

one-stage prothrombin test. Russell's viper venom is insensitive to changes in factor VII, and does, in fact, possess a factor VII-like activity (Jenkins, 1954*b*). It requires lipoid when used as a source of thromboplastin (Macfarlane, Trevan and Attwood, 1941), and this explains the prolonged prothrombin time obtained with normal plasma when this substance was used without the addition of lecithin. The patient's plasma may have possessed more lipoid than the normal control, which would account for the faster prothrombin time. When lecithin was added, both the patient's plasma and normal plasma gave a prothrombin time of six seconds.

The two-stage prothrombin estimation showed the patient to possess normal quantities of prothrombin. However, thrombin was generated more slowly, a flatter than normal curve being obtained with a delayed peak of thrombin generation. This is the type of curve found in factor VII or factor V deficiencies.

The patient's plasma therefore reacted with brain extracts and with Russell's viper venom in the same manner as factor VII-deficient plasma. Further one-stage prothrombin tests showed that the addition of "Dindevan" plasma reduced the defect slightly, but did not correct it, and that the patient's serum improved the result obtained with "Dindevan" plasma, but not so much as normal serum. The fact that these two types of deficiency were not mutually corrective shows that they must be identical in their reaction with brain extracts.

Factor VII is known to be required for the adequate generation of thromboplastin (Biggs and Douglas, 1953*b*), and for this reason the thromboplastin generation test and the prothrombin consumption test were carried out. The patient's prothrombin consumption was normal, which suggested that the generation of thromboplastin was unimpaired. Unfortunately it is not possible to carry out prothrombin consumption studies on "Dindevan"-treated patients, as prothrombin itself is deficient in these cases together with factor VII. The generation of thromboplastin in the patient's blood was normal when tested by the thromboplastin generation test; this supports the assumption made from the prothrombin consumption studies. The ability of the patient's blood to generate thromboplastin normally contrasts strikingly with the impaired generation of thromboplastin of patients treated with dicoumarol and its derivatives. It is also interesting to note that not only could the patient's own platelets, aluminium hydroxide-treated plasma and serum, when mixed together, generate thromboplastin normally, but that the patient's own plasma reacted with this thromboplastin equally well as with that generated by reagents from normal subjects. It would appear from this test and from the results of the thrombin generation test that there was no abnormality in the patient's intrinsic coagulation mechanism. However, although the patient's plasma reacted normally with blood thromboplastin, it was unable to do so with brain extracts. The defect could have been attributed to a species specificity had it not been noted with both human and rabbit brain preparations.

We have, therefore, a patient with a coagulation defect resembling that due to a factor VII deficiency in its reactions with brain extracts and Russell's viper venom, but differing greatly from it when thromboplastin generation studies were employed.

Other cases in which prolonged one-stage prothrombin times were corrected by the addition of serum have been reported as factor VII deficiencies. In three such cases (Frick and Hagen, 1953; Alexander, Goldstein, Landwehr, and Cook, 1951; Owren, 1952) prothrombin consumption was found to be normal, which suggests that here also the generation of thromboplastin was unimpaired. In the case described by Alexander, Goldstein, Landwehr and Cook (1951) the addition of dicoumarol plasma was found to reduce but not correct the defect. It is therefore possible that some of these cases may have been identical with the one described in this paper.

Summary.

A case of a congenital coagulation deficiency disorder is presented; the patient was a girl, aged sixteen years. The condition resembled a factor VII deficiency as far as reactions with brain extracts and Russell's viper venom were concerned, but did not result in the defective thromboplastin generation found in the blood of patients treated with dicoumarol and its derivatives.

Acknowledgements.

I should like to thank Dr. Rosemary Biggs, Oxford, for her interest and many helpful suggestions. I am also indebted to Dr. R. F. West for permission to publish the case, and to Dr. J. A. Bonnin and Professor H. N. Robson for help in the preparation of the paper. Miss M. Jenner provided valuable technical assistance.

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Reviews.

The Year Book of the Eye, Ear Nose and Throat (1954-1955 Year Book Series); The Eye, edited by Derrick Vail, B.A., M.D., D.Oph. (Oxon.), F.A.C.S., F.R.C.S. (Hon.); The Ear, Nose and Throat, edited by John R. Lindsay, M.D.; 1955. Chicago: The Year Book Publishers, Incorporated. 8" × 5½".

THIS Year Book covers the ground of its subject matter without much fuss. It contains abstracts of articles taken from journals received by the editors between January and December, 1954. With a limited amount of editorial comment the editor of the section on "The Eye", Derrick Vail, has divided his material in chapters dealing with the orbit and adnexa, the conjunctiva and cornea, the uvea, refraction and motility, the lens and cataract, neurology and visual fields, the retina, glaucoma, surgery, therapy and miscellaneous subjects.

John R. Lindsay, editor of the section on "The Ear, Nose and Throat", deals first with the ear, dividing the material into chapters on vestibular function and vertigo, hearing and hearing tests, tubal function and *otitis media*, otosclerosis and fenestration, facial paralysis, salivary glands and miscellaneous subjects. The abstracts dealing with the nose and throat are grouped under the headings of the nose and sinuses, the oropharynx and nasopharynx, the larynx and hypopharynx, the trachea, bronchi and œsophagus, allergy and miscellaneous subjects.

This book will be useful not only to specialists in the fields concerned, but also to general practitioners and others who wish to be kept informed of worthwhile information being published in specialist journals outside their normal range of reading.

Stone in the Urinary Tract. By H. P. Winsbury-White, M.B., Ch.B.Ed., F.R.C.S.Ed., F.R.C.S. (England); Second Edition, 1954. London: Butterworth and Company (Publishers), Limited. Sydney: Butterworth and Company (Australia), Limited. 10" × 7", pp. 352, with 144 illustrations, a few in colour. Price: 86s. 6d.

MR. WINSBURY-WHITE has produced a second edition of this book after an interval of almost twenty-five years. It is considerably enlarged and is undoubtedly the most complete work now available on calculus disease in the urinary tract. It is profusely illustrated and, as it is based on the personal experience of almost 900 patients, some of the pictures are unique.

The subject matter is primarily surgical in character, but the chapters on ætiology, non-operative treatment and calculus in pregnancy and children are of interest to physician and surgeon alike.

The historical section is of great interest, recording in detail the operative treatment of vesical calculus in the past.

There is an extensive review of the ætiological factors in stone formation, most of it largely theoretical in nature. The author stresses the importance of dietary factors and continued low-grade infection. Not all urologists would agree that these are primarily the cause of stone formation. We could find no mention of nephrocalcinosis.

In the management of multiple and bilateral renal calculi, a most useful section of the book as it is based on experience of so many personal cases, the author stresses the necessity for lateral radiography and pyelography in diagnosis. These views we are often apt to omit.

The criteria for surgery and the various surgical approaches are well described. The author does not, however, discuss partial nephrectomy or heminephrectomy for upper calyceal stone. In the section on ureteric calculus he is obviously keen on using the wax-coated bougie in diagnosis, but he does not mention the Ainsworth Davis corkscrew, the loop catheter or the basket in manipulative extraction.

The book has a most extensive bibliography and will be read with the greatest of interest by all urologists.

X-Ray Atlas and Manual of Esophagus, Stomach and Duodenum. By T. J. J. H. Meuwissen, with an introduction by Robert D. Moreton, M.D., F.A.C.R.; 1955. Amsterdam: Elsevier Publishing Company. London: Cleaver-Hume Press, Limited. 11" × 8", pp. 702, with 1201 illustrations. Price: £8 15s.

THIS work by a Dutch author has been received from the publishers, Elsevier of Amsterdam. It is unusual to receive works of this nature from the Continent. There is quite an amount of text, in addition to the atlas with its illustrations, which is unusual in similar works by British and American authors. The various organs are considered fully as regards anatomy and physiology and many excellent drawings of the various structures are given and many pathological lesions are described. A condition rarely seen here is dysphagia accompanying idiopathic hypochromic anæmia; it is common in women and frequently is a forerunner of malignant disease. The anæmia is accompanied by a reduction in the iron content of the blood, with changes in the tongue and fingers. Congenital abnormalities are well illustrated. The main part of the work consists of reproductions of films of practically every lesion met with in these organs, with a description of the plates on the opposite page, together with operative or post-mortem findings. The pictures are mounted on a light cream background which rather enhances detail. Most of the illustrations are from "spot films". There is a tendency to include too many pictures of almost identical lesions. Many good films show the changes in ulcer when carcinoma has developed in them. In the duodenal section there is a tendency also to reproduce too many films of almost identical conditions. The section on the post-operative stomach is rather disappointing, as it is too condensed and does not deal extensively enough with the appearances after proximal end interference, or the results of operation for hiatus conditions.

Altogether this is a most interesting work, especially for reference when unusual conditions are met with. It should be of particular value to men with limited X-ray experience and should find a place in the bookcase of all workers.

The Year Book of Urology (1954-1955 Year Book Series), edited by William Wallace Scott, M.D., Ph.D.; 1955. Chicago: The Year Book Publishers, Incorporated. 8" × 5½", pp. 372, with 83 illustrations. Price: $6.00.

THIS Year Book is made up of abstracts of articles dealing with urological subjects taken from a variety of special and general journals received by the editor between November, 1953, and October, 1954. An opening section on general considerations has subsections on infections (including gonorrhœa), calculi, urography, instruments and appliances, and miscellaneous subjects. Matters dealt with in a section on the kidney include anomalies, tumours, tuberculosis, trauma, renal failure, nephritis and nephrosis, hypertension, physiology, transplantation and hydronephrosis. The section on the adrenals contains material on the adrenogenital syndrome and cortical tumours, medullary tumours, and adrenalectomy for hypertension and cancer. In the section on the ureter are subsections on anomalies, calculi and uretero-intestinal anastomosis. Articles dealing with the bladder are grouped under the headings of tumours, micturition, neurogenic bladder, trauma and surgical technique. Articles relating to the prostate deal with prostatitis, prostatectomy, calculi and carcinoma. The final section, which is concerned with the genitalia, has subsections on the penis, the urethra (including treatment of gonorrhœa and strictures), hypospadias, testis tumours, scrotal swellings, epididymides, vasa and seminal vesicles, fertility and sterility, and cryptorchidism. This Year Book will be of value to urologists, general surgeons, general practitioners and others who wish to keep themselves informed of current advances in urology.

Ciba Foundation Colloquia on Endocrinology: The Human Adrenal Cortex. Edited by G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch., and Margaret P. Cameron, M.A., A.B.L.S., assisted by Joan Etherington; 1955. London: J. and A. Churchill, Limited. Volume VIII. 8" × 5½", pp. 620, with 227 illustrations. Price: 55s.

VOLUME VIII of the Ciba Foundation Colloquia on Endocrinology deals with the human adrenal cortex. The volume contains papers and discussions presented at two colloquia, one on histological and biochemical aspects and cortico-

medullary relationships, the other on physiological and pathological aspects and hypothalamic and pituitary relationships. The first meeting was attended by 33 specialists from Europe and America and the second by 34 specialists not all the same as those at the first meeting. The papers cover a very wide range of subjects. In all, 34 papers were given and after each there was a discussion. It is impossible even to list the titles here, much less consider them in any detail. The text occupies 653 pages. Most of the papers are difficult to read and the discussions indicate that differences of opinion about interpretation are usual. Many of the papers, especially in the second part, have considerable clinical interest. It would seem that almost everything that is known about the adrenal cortex and its activities, except the chemistry of the steroids, which has been dealt with in an earlier volume, is contained in this volume with a great deal that is surmised. The book is a thoroughly authoritative one and the discussions draw attention to points that have not been cleared up. It can be recommended to anyone needing a detailed account of the present position in regard to the adrenal cortex and its functions.

Biochemical Investigations in Diagnosis and Treatment. By John D. N. Nabarro, M.D., M.R.C.P.; 1954. London: H. K. Lewis and Company Limited. 8½" × 6", pp. 308, with five illustrations. Price: 25s.

BOOKS on the application of biochemical methods for clinical purposes are usually written by biochemists. They necessarily approach the subject from the standpoint of the laboratory worker. Dr. J. D. N. Nabarro, however, is a physician. His approach is from the clinical aspect of the subject. He asks the questions: "Is such and such a test likely to be useful?" "Is it practicable?" This is the typical approach of the British clinician. It is perhaps partly due to the necessity for efficient use of limited laboratory facilities. Dr. Nabarro's answer to one or both of his questions is often in the negative.

The book is divided into fourteen chapters, the first four of which deal with water and electrolyte balance and inorganic constituents of the body. Another group of chapters deals with disturbances of metabolism of protein, carbohydrate and fat. Two chapters deal with diseases of the gastro-intestinal tract and associated organs, and there are chapters on renal function, cerebro-spinal fluid, endocrine glands, vitamins, and some common forms of poisoning. Each chapter includes a selected list of references.

At the end of the book are several tables of normal values of biochemical findings, and their ranges of variation. These tables are subdivided into those of tests usually carried out in hospital laboratories, and tests not usually carried out. There are three pages of references to the tables. The book also contains a comprehensive general index. This is very easy to use as it is divided into two parts, an index of investigations and one of conditions.

A book like Nabarro's has long been needed. It deals critically with the use and interpretation of a very wide range of biochemical tests. It should prove invaluable to the clinician and to the laboratory worker. To the latter it is both salutary and encouraging.

CORRIGENDUM.

IN the review of "The Skin: A Clinicopathological Treatise", by Arthur C. Allen, on July 2, 1955, the condition of keratoacanthoma or self-healing epithelioma was erroneously stated to have been omitted. We regret this error. The condition is discussed under the term "So-called 'Self-Healing Squamous Cell Carcinomas'", and it is adequately described on page 748 and illustrated in plate 320. It is the belief of Allen that these lesions are pseudo-epitheliomatous hyperplasia in the lining of comedos or inclusion cysts. With this view we agree.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Obstetrics", by J. P. Greenhill, M.D.; Eleventh Edition; 1955. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical), Limited. 10" × 7", pp. 1096, with 910 illustrations, 144 in colour. Price: £7.

The first edition was published in 1953.

"Electrochemistry in Biology and Medicine", edited by Theodore Shedlovsky; sponsored by The Electrochemical Society, Incorporated, New York; 1955. New York: John Wiley and Sons, Incorporated. London: Chapman and Hall, Limited. 9" × 6", pp. 382, with many illustrations. Price: $10.50.

This book had its origin in a symposium on electrochemistry in biology and medicine held in April, 1953. There are 23 contributors.

"Morbidity in the Municipal Hospitals of the City of New York: Report of an Exploratory Study in Hospital Morbidity Reporting", by Marta Fraenkel, M.D., and Carl L. Erhardt; 1955. New York: Russell Sage Foundation. 9" × 6", pp. 230, with 56 tables. Price: $4.50.

"A pilot study . . . to test a plan for hospital morbidity reporting and to evaluate data thus obtained."

"The Medical Clinics of North America"; 1955. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical), Limited. New York Number. 9" × 6", pp. 308, with 139 illustrations. Price: £8 2s. 6d. per year in cloth binding and £6 15s. per year in paper binding.

This number consists of a symposium on the basic sciences in medical practice.

"The Year Book of Pathology and Clinical Pathology (1954-1955 Year Book Series)", edited by William B. Wartman, B.S., M.D.; 1955. Chicago: The Year Book Publishers, Incorporated. 7½" × 5", pp. 486, with 168 illustrations. Price: $6.00.

One of the "Practical Medicine Series of Year Books".

"Anatomy and Physiology for Nurses", by W. P. Gowland, M.D. (Lond.), F.R.C.S. (Eng.), and John Cairney, D.Sc., M.D., F.R.A.C.S.; Fourth Edition; 1955. Christchurch: N. M. Peryer, Limited. 8½" × 5½", pp. 472, with 199 illustrations. Price: 45s.

The first edition was published in 1941.

"A Manual of Psychiatry", by K. R. Stallworthy, M.B., Ch.B.; Third Edition; 1955. Christchurch: N. M. Peryer, Limited. 7½" × 5", pp. 334. Price: 30s.

Intended for general practitioners of medicine and for nurses.

"Symposium on Atherosclerosis", held under the auspices of The Division of Medical Sciences, National Academy of Sciences, and National Research Council; at the request of The Human Factors Division, Air Force Directorate of Research and Development (March 22-23, 1954). Washington: National Academy of Sciences, National Research Council. 10" × 6½", pp. 250, with many illustrations. Price: $2.00.

The book is divided into five sections, each of which is provided with a summary. There are 23 papers with discussions.

"Principles of Medical Statistics", by A. Bradford Hill, C.B.E., D.Sc., Ph.D., F.R.S.; Sixth Edition; 1955. London: The Lancet, Limited. 8½" × 5", pp. 324. Price: 10s. 6d.

Comprises a series of articles reprinted from *The Lancet*.

"Annual Review of Medicine", edited by David A. Rytand, M.D.; Volume VI; 1955. Stanford: Annual Reviews, Incorporated. 9" × 6", pp. 474. Price: $7.00.

There are 25 chapters, each of which deals with a separate subject. The work is well documented.

"Psychology in Nursing", by Wendell W. Cruze, Ph.D.; 1955. New York: The Blakiston Division, McGraw-Hill Book Company, Incorporated. 9" × 6", pp. 504, with 79 illustrations. Price: $5.50.

Deals with the fundamental principles of psychology and their practical value to the nurse.

"Diseases of the Liver and Biliary System", by Sheila Sherlock, M.D. (Edin.), F.R.C.P. (Lond.); 1955. Oxford: Blackwell Scientific Publications. 9" × 5½", pp. 734, with 158 illustrations. Price: 50s.

Intended for physicians, surgeons and pathologists, and as a reference book for the clinical student.

"Neuroglia Morphology and Function", by Paul Glees, M.A., D.Phil., M.D.; 1955. Oxford: Blackwell Scientific Publications. 8½" × 5½", pp. 124, with 44 illustrations. Price: 25s.

This is a review of the available literature on neuroglia with the author's own observations on the subject.

The Medical Journal of Australia

SATURDAY, AUGUST 27, 1955.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of the article. The abbreviations used for the titles of journals are those adopted by the Quarterly Cumulative Index Medicus. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

POLIOMYELITIS AND TONSILLECTOMY.

THE relationship between poliomyelitis and tonsillectomy is still not settled despite many investigations and a great deal of discussion, particularly in the United States of America. At the same time a significant association between tonsillectomy and the bulbar manifestations of poliomyelitis is generally accepted. Important evidence on this last-mentioned point was brought forward in 1952 by R. V. Southcott, of South Australia, in a paper read at the eighth session of the Australasian Medical Congress (British Medical Association),[1] and by F. H. Top, in the United States.[2] Southcott's observations have been amplified in subsequent papers.[3] Now a report has been published by the Medical Research Council Committee on Inoculation Procedures and Neurological Lesions,[4] in which it is stated, curiously enough, that no extensive study of the association between poliomyelitis and tonsillectomy has previously been made in England and Wales. The report deals separately with recent and with remote tonsillectomy.

The first part of the report is based on information obtained about all patients in England and Wales from early in 1951 to the end of 1953 said to have had their tonsils removed within the three months before the onset of poliomyelitis. After elimination of a small number of cases in which the available information was unsatisfactory, 103 were studied. The patients were children aged up to eighteen years who developed poliomyelitis within 91 days after tonsillectomy; 61 (59%) had symptoms within three weeks after tonsillectomy. The report states that the concentration was most evident in the bulbar and bulbo-spinal groups, in which 79% of cases occurred within three weeks after operation, compared with 38% of spinal cases and 31% of non-paralytic cases. It is pointed out that a growing number of American observers agree that more patients with a history of tonsillectomy within a month before the onset of poliomyelitis develop the bulbar form of the disease than can be explained by chance, but that they have some doubt about the association between spinal forms of the disease and recent tonsillectomy. The observations in the present report support these conclusions. The comment is made that tonsillectomy as practised at present added relatively few to the total number of cases reported during the study, but tonsillectomy should continue to be restricted in any area where the disease is unusually prevalent. As a community problem the situation is relatively minor; for the individual whose tonsils are removed the problem is important.

Turning to the question of remote tonsillectomy, the report presents data collected in selected areas of England and Wales between the middle of 1951 and November, 1953. Records were obtained of the history of tonsillectomy at any time before the onset of paralytic poliomyelitis in 51 patients under five years of age and in 203 patients aged from five to fifteen years. Histories were similarly obtained for the same number of matched controls. In the under five years age group only two of the patients and none of the controls had had their tonsils removed. In the five to fifteen years age group 72 (35%) of the patients had undergone tonsillectomy compared with 44 (22%) of the controls; the differences between patients and controls were greatest in the group with bulbar paralysis, intermediate in the group with bulbo-spinal paralysis and least in the group with spinal paralysis. In the bulbar and bulbo-spinal groups, most patients had had their tonsils removed one year, and it was often five years or more, before the onset of poliomyelitis. The report thus, quite reasonably, concludes that within the limited age range of the study the removal of tonsils even five or more years before the onset of symptoms would appear to render patients with poliomyelitis more liable to develop the bulbar or bulbo-spinal form of the disease than the spinal-paralytic form. These findings are in line with those of major studies in North America and with those of Southcott in South Australia, and serve to associate an additional long-term hazard with tonsillectomy. The report considers certain factors that could make indirect the apparent association between remote tonsillectomy and bulbar poliomyelitis. For example, the type of child who is liable to have his tonsils removed may also be the type who is most likely to develop bulbar paralysis. This could occur in children of well-to-do parents or in older children, who have had greater opportunity for operation. These possibilities, however, seem to be ruled out by the control scheme of the study, which matched controls and patients for age, sex and social position. Another factor could be some local condition in the pharynx which on the one hand provided an indication for tonsillectomy and on the other made the child more liable to bulbar poliomyelitis even after the operation. However, this factor (as well as those of age

[1] M. J. AUSTRALIA, October 4, 1952.
[2] *J.A.M.A.*, October 11, 1952.
[3] M. J. AUSTRALIA, August 22, 1953, November 27, 1954, and December 4, 1954.
[4] *Lancet*, July 2, 1955.

and sex) has been examined carefully by G. W. Anderson and J. L. Rondeau,[1] and it seems to be of little significance. On present information, therefore, the Medical Research Council Committee's report concludes that the removal of tonsils has been responsible for the development of bulbar or bulbo-spinal poliomyelitis by some children who would not otherwise have had it.

The problem thus remains of deciding the wisdom or otherwise of tonsillectomy in an individual case. The consensus of opinion seems to be that the risk associated with poliomyelitis should not be allowed to outweigh a genuine threat to a child's health from diseased tonsils. If poliomyelitis is unusually prevalent, extra caution is justified in assessing the indications for tonsillectomy. On the other hand, the restraint imposed by the thought of poliomyelitis, whether the local incidence is particularly high or not, provides a healthy reinforcement to the modern inclination, on other grounds, to discourage indiscriminate tonsillectomy.

THE DUTY OF DOUBT.

IN the practice of medicine it is fatally easy to accept a single observation or group of observations and to draw general conclusions from it or them—the *post hoc* readily becomes the *propter hoc*. Medical folk often attribute an attitude of that kind to people who have received no medical or other scientific training, and of the general existence of such an attitude the practitioner has evidence constantly thrust before him. But it is with the doctor himself that we need to be chiefly concerned; doubt or scepticism with him is a duty. He uses, and indeed has to use, empirical methods so often that he may forget the true basis of much of his work. Increase in knowledge comes primarily from observation. Observation, properly used, may carry us a long way. The late Wilfred Trotter pointed out long ago[2] that the range and precision have been increased by instruments of various kinds, that completeness and exactitude of record have increased its trustworthiness and that mathematics has given it the power of detecting relations among recorded facts too complex or too obscure to be within range of direct contemplation. In spite of all this, observation must have its limitations and this is where experiment comes into the picture. We need not discuss experiments on animals or man; it must suffice to observe that, in the words of Trotter, experiment "isolates the event to be studied from the common order of nature, and causes it to occur in circumstances as far as possible simplified and subject to specification". We then ask whether the duty of scepticism ceases when experiment appears to confirm conclusions drawn from certain observations. A sceptic has been described as not one who doubts, but one who examines. Of course we know that an urge to examine comes from feelings of doubt, and Cicero it was who declared that by doubting we arrived at the truth. We must conclude that not even with the results of experimentation in our hands are we absolved from the duty of doubt or scepticism. To misapply the findings of an experiment, even in a restricted field, may be as easy as it is to accept observations at their face value. Further, experimental results may tell only part of a story and more work be needed. It is possible to go to extremes when we deal with the opinions and apparently serious work of respected investigators who are, shall we say, over-enthusiastic, and we may remark, as one learned teacher did on a celebrated occasion, that we have passed the age when we are "interested in fiction". But we need not do so. We shall not go far wrong if we keep before our minds what is implied in the maxim of that great investigator Claude Bernard: "True science teaches us to doubt and, in ignorance, to refrain."

[1] *J.A.M.A.*, July 24, 1954.
[2] *Brit. Med. J.*, July 26, 1930.

Current Comment.

OSTEOPOROSIS.

THERE is still much confusion in the naming of metabolic bone diseases, and a wrong naming often leads to wrong treatment. A. M. Cooke,[1] in the Lumleian lectures for 1955, sets out clearly and in detail the meaning of the term osteoporosis, the relation of this condition to other bone diseases, its causation and its treatment. The paper is important, and it will be worth while to record the following main points drawn from it. The general term decalcification is used to describe X-ray appearances or post-mortem findings in which the bones appear to be deficient in mineral salts, or are unduly thin, soft or brittle. These changes may be due either to too little bone substance or to inadequately calcified bone matrix. Cooke defines osteoporosis as "deficiency of bone arising from insufficient matrix formation, in the presence of normal calcification of osteoid tissue". The condition of bone arising from deficiency of calcium or vitamin *D* or both, with a clear clinical picture, X-ray changes, biochemical findings and histological features, he classes as osteomalacia. In osteoporosis the histological picture is that there is simply too little bone, the trabeculæ are fewer and thinner than normal, and this leads, in the spine, to shrinkage and compression of the centre with biconcave bodies and kyphosis. The terms senile osteomalacia and post-menopausal osteomalacia have no meaning, for a patient either has or has not deficient calcification of osteoid tissue. They are, however, often used as synonyms for osteoporosis. Many causes have been suggested for osteoporosis. Except in the grosser deficiencies of protein and mineral intake or absorption, it is doubtful if malnutrition is a common cause of osteoporosis. Pregnancy makes considerable demands on the mother for protein, calcium and phosphorus, and various authors have adduced evidence that multiparous women are much more likely to have osteoporosis than nulliparous. There may well be endocrine factors here. Ovary, testis, parathyroid gland, adrenal body and pituitary gland all influence bone growth in one way or another. Œstrogens lead to hyperossification if given in large doses or over a long period. The testis is important in the formation of bone matrix. Long-continued over-activity of the thyroid often leads to osteoporosis. The relation of the parathyroids to osteoporosis is not clear. Adrenal function is necessary for normal bone formation. Osteoporosis is extremely common in Cushing's disease; indeed the disease used to be called osteoporotic obesity. In acromegaly there is often osteoporosis.

Mechanical factors play a very large part in the induction of osteoporosis, particularly immobilization of the patient. Local osteoporosis in the limbs of patients immobilized for the treatment of tuberculous joints is very common. Increased loss of nitrogen in the urine is found after any form of injury, but is much greater in patients with fractures than in those with comparably severe non-osseous injuries. The nitrogen loss is paralleled by the

[1] *Lancet*, April 30, 1955.

calcium loss; both are greater when the patient is immobilized in plaster, and they fall together rapidly when the plaster is removed. Apparently the absence of normal stresses and strains removes some of the stimulus to bone formation by osteoblasts, while normal resorption by osteoclasts continues unchecked. These factors are more important in the aged than in the young. The amount of exercise required to prevent these osteoporotic troubles seems to be remarkably small.

The symptoms of osteoporosis vary from none at all to complete incapacity from severe pains. The pains are mainly in the back, radiating round the trunk and to the buttocks and down the legs. These are usually aggravated by movement or jarring. Compression of the spinal cord does not occur, in spite of skeletal deformities. The physical signs vary from none to gross spinal deformity. Kyphosis is the commonest. The X-ray picture is characteristic with poor contrast between bones and soft tissues, but the difficulties of determining the degree of osteoporosis by X-ray examination are great. If there are X-ray changes indicating osteoporosis, and particularly if vertebral collapse is present, there must be gross anatomical changes. Osteoporosis is, strictly speaking, a histological diagnosis and can be made with certainty only by the morbid anatomist. Certain clinical features and the X-ray changes are often sufficiently well defined to justify a bedside diagnosis. If a patient of over sixty years of age has pains in the trunk or legs for which there is no obvious explanation, osteoporosis should be considered, especially if the patient is a woman. Loss of height, evidence of shortening of the axial skeleton, a rounded kyphosis, a transverse infolding of the skin across the upper part of the abdomen and approximation of the lowest ribs to the pelvis are important signs. Cooke found in his series of patients that the serum calcium, plasma phosphorus and plasma phosphatase content were all within normal limits—a diagnostic point of importance. Osteoporosis is extremely common, but is hardly mentioned in text-books of medicine. In senile osteoporosis at least there is an endocrine component which is treatable.

For treatment Cooke recommends that the patient should be got out of bed and, if the pains are severe, given a light spinal jacket. A diet with a high protein content and milk should be given to supply the materials necessary for bone formation. Male and female sex hormones should be given, generally in mixture, but not in large doses, and, preferably, intermittently. Patients should be treated for long periods. This treatment generally gives great subjective improvement and improvement in function, but seldom is the X-ray appearance of the bones much altered.

CŒLIAC DISEASE AND WHEAT GLUTEN.

THE notable work on cœliac disease being done at the University of Birmingham has been referred to in these columns from time to time. In the most recent reference[1] mention was made of two children in a series who had normal pancreatic function associated with steatorrhœa, but who failed to yield the usual favourable response to a gluten-free diet. It appeared that some special ætiological factor was involved in these cases, and the question has now been further investigated by the Birmingham workers. The purpose of the study, which is reported by C. A. C. Ross, A. C. Frazer, J. M. French, J. W. Gerrard, H. G. Sammons and J. M. Smellie,[2] was to determine what proportion of children presenting with active cœliac disease responded to a diet free from wheat gluten, and to examine the ætiology of the disorder in those children who did not respond. The main criterion for inclusion in the series studied was the presence of chronic steatorrhœa with normal pancreatic function. The main therapeutic criterion was disappearance of the steatorrhœa. Of the 30 children in the series 28 responded to a diet free from wheat gluten; and as they had been ill for several months before treatment, their recovery on the diet is regarded as strong evidence in favour of the ætiological relationship of wheat gluten to their illness. More precise evidence of this relationship was provided by the reappearance of steatorrhœa on reintroduction of wheat gluten into the diet of 12 of the 28 children. It may be noted also that in children who responded to the gluten-free diet, improvement in fat absorption coincided with improvement in chylomicrograph, in standard weight for age and in hæmoglobin level, and with dimunition in the dilatation of the small intestine, but not with any significant improvement in the findings of the glucose tolerance test.

The failure of two children to respond to the gluten-free diet, with the similar finding in another series already referred to, indicates that factors other than gluten may, in a limited number of cases, be responsible for the signs and symptoms of cœliac disease. One of the two children responded to treatment with bile, and her condition is regarded as being due to a deficiency of bile salts. It is of interest to note, as Ross and her colleagues point out, that deficiency of bile salts has been proposed as the cause of cœliac disease by various workers over the past half-century. Apparently it is "a" cause, although not "the" cause.

The other child's symptoms seem to have originated from an attack of gastro-enteritis in infancy. The occurrence of vomiting after a meal containing a moderate amount of fat, together with radiological evidence of gastric stasis associated with a barium meal containing fat, suggested that oral administration of fat resulted in pylorospasm. The cause of the steatorrhœa, however, remains obscure. It is stated that one of the two children in the other series mentioned had a similar history, and it appears that in each case after an attack of gastro-enteritis the child had not regained the ability to assimilate fat. In this connexion attention is drawn to the fact that after gastro-enteritis reintroduction of fat into an infant's feeds often needs to be gradual.

This study is of great interest for the further light it throws on the causation of cœliac disease. In the vast majority of cases gluten appears to be the major causative factor, and understanding of this has transformed the management of the condition. At the same time, in certain cases, other factors are responsible, and this helps to bring into perspective findings and theories of earlier investigators which do not line up with the gluten aspect. It would probably be a good idea to adopt the suggestion made by the Birmingham group in this paper that the disorder which responds to a gluten-free diet should be regarded as a separate entity and that it be called "gluten-induced cœliac disease".

[1] M. J. AUSTRALIA, April 16, 1955.
[2] *Lancet*, May 28, 1955.

SYNTHETIC STEROIDS AND RHEUMATOID ARTHRITIS.

METACORTANDRACIN ("Prednisone") and Metacortandralone ("Prednisolone") are synthetic steroids, modifications of the cortisone nucleus, developed for use in rheumatoid arthritis. J. J. Bunim, M. M. Pechet and A. J. Bollet[1] reported that they possess three to four times the activity of cortisone or hydrocortisone, and that initial courses of from 30 to 60 milligrammes daily, divided into three equal doses, and then gradually reduced after fourteen days until a minimum maintenance dose was reached, produced significant lessening of all symptoms and increased range of motion. Biopsy of synovial membrane showed considerable subsidence of inflammation. The erythrocyte sedimentation rate was restored to normal. There were significant increases in the hæmoglobin level and red and white blood cell counts, neither sodium retention nor potassium or nitrogen loss occurred, and there were only minor side effects.

[1] *J.A.M.A.*, January 22, 1955.

J. R. Dordick and E. J. Gluck,[1] in a report on eleven patients treated with "Prednisone", stated that all patients demonstrated an effective, fast and dependable anti-rheumatic or anti-inflammatory response, without serious side effects. There was relapse when the drug was discontinued. H. M. Margolis, J. H. Barr, B. L. Stolzer, C. H. Eisenbeis and E. W. Martz[2] state that "Prednisone" is capable of producing anti-rheumatic effects in smaller doses than those required with cortisone and hydrocortisone; moreover, it does not cause water retention; and has been reported to have a favourable effect on the anæmia which sometimes accompanies rheumatoid arthritis. The paper ends, however, with a warning that its diabetogenic properties require further investigation.

In the same issue of the journal A. J. Bollet, R. Black and J. J. Bunim report that in two patients treated with "Prednisone" and "Prednisolone" and in one treated with "Prednisone" alone, a duodenal ulcer developed, and one patient developed a depressive psychosis. The ulcers were asymptomatic, and were discovered only as a result of periodic X-ray examinations undertaken as part of a general study of the patients' reactions. These three patients were members of a group of 18 in this study, so that the incidence of ulceration is high, and the fact that it was asymptomatic suggests that a warning for care in using these drugs is very necessary.

THE PRESERVATION OF OPHTHALMIC SOLUTIONS.

THE preservation and sterilization of eye drops are usually neglected, especially by the practitioner who uses ophthalmic drugs only occasionally, and this means that bottles of drops may be retained for months on end. The importance of the subject is underlined by the appearance within several months of three papers on the subject by G. E. Lawrence,[3] by M. L. Frith and S. E. Wright,[4] and by R. F. Lowe.[5]

In ophthalmic solutions lacking antibacterial activity microbial contamination can be expected once the container has been opened. The applicator will be exposed to extraneous materials such as dust, water and so forth, if the dropper is placed after use on a table or stored on a shelf in a medicine cabinet. Another source of contamination is contact of the dropper with an infected surface of the eyelid or the eye of the patient. This would occur most often in the consulting room. Unless some preservative is added one can expect a contaminated ophthalmic solution once the container is opened and used. The most objectionable contaminants are organisms of the Pseudomonas and the Proteus groups, both of which can cause serious ophthalmic infection and are extremely resistant to present forms of chemotherapy. A careful review of the literature by Lawrence reveals that in the dispensing of ophthalmic drugs, chlorobutanol, phenylmercuric nitrate and benzalkonium chloride are considered the bacteriostatic agents most suitable for providing "self-sterilizing" solutions. Frith and Wright, on the other hand, from their experiments found that cetrimide ("Cetavlon") one in 20,000 is the most suitable preservative. It destroys common pathogenic bacteria, it is compatible with most chemicals in ophthalmology, and it is non-irritating. The interests of the patients and practitioners in Australia have been guarded in this respect as Lowe has indicated. A new Australian and New Zealand pharmaceutical formulary now in the press has been drawn up with the section on the formulation of eye drops rewritten to include the modern concepts. Much thought has been given to ophthalmic drops with special reference to the active medicaments, preservatives, buffers, isotonicity, corneal penetration and viscosity. However, in spite of the addition of a chemical to sterilize solutions, one must remember that the "ideal" preservative is yet to be discovered, and all care should be exercised to prevent contamination of the eye drops.

[1] *J.A.M.A.*, May 21, 1955.
[2] *J.A.M.A.*, June 11, 1955.
[3] *Am. J. Ophth.*, March, 1955.
[4] *Brit. J. Ophth.*, March, 1955.
[5] *Tr. Ophth. Soc. Australia*, Volume XIV, 1954.

LUNG BIOPSY.

DIFFUSE PULMONARY DISEASE often exists without presenting specific signs and symptoms, and long investigation by ordinary methods may fail to provide a definitive diagnosis; a quick method of making a lung biopsy would be welcome in these cases. P. A. Theodos, F. F. Allbritten and R. L. Breckenridge[1] have reported on their results; they used a method originated by K. P. Klassen and his colleagues. Local infiltration anæsthesia is used, and before the chest is opened the patient is given a trial run with a positive pressure oxygen mask to ensure that he will know how to do his part. The site of biopsy is chosen over an area showing good X-ray evidence of disease, preferably anteriorly because of the wider intercostal spaces. The incision is made over this site, the muscles are split down to the intercostal space, and the intercostal muscles are divided so as to expose the parietal pleura. The mask is then applied to the patient's face and the oxygen turned on—positive pressure is needed to keep the lung expanded. The pleura is opened and the lung grasped with Allis forceps; palpation over a limited area is possible, so that the best site for biopsy can be chosen. This area is demarcated by mattress sutures, the desired portion is excised, and the sutures are tied off. The wound is checked for bleeding and air leaks, and when none remain the lung is allowed to resume its position, still expanded by the positive oxygen pressure; the chest opening is then closed. Theodos and his colleagues report having achieved specific diagnosis in 27 out of 50 cases by biopsy of lung tissue secured by this method; complications of the operation were remarkably few and quite unimportant, except that one patient who had silicosis and myocardial degeneration developed a small pneumothorax after operation and subsequently died of cardiac failure secondary to pulmonary insufficiency. It is claimed that the procedure, by providing a rapid method of accurate diagnosis, reduces hospitalization time and expense due to many alternative methods of diagnosis, offers in many cases the only final decision on medico-legal aspects (especially in compensation claims for silicosis) and provides reliable data for the making of a prognosis. If the effects of the operation can be kept as innocuous as these workers have kept theirs, the method should be of great value in selected cases.

CITRIC ACID INTOXICATION.

REPLACEMENT TRANSFUSION and massive transfusions in patients with severe shock involve the incidental administration of relatively large amounts of sodium citrate and citric acid, and the question has arisen of how much harm this can do; it was raised recently at a meeting of the New South Wales Branch of the British Medical Association. J. P. Bunker, J. B. Stetson, R. C. Coe, H. C. Grillo and A. J. Murphy,[2] have investigated the levels in the serum of citrate, calcium, protein, magnesium and potassium in 130 adult patients receiving ordinary and large transfusions with citrated blood. They found that normal patients who were given blood at the rate of not more than 500 millilitres every thirty minutes gave no evidence of citric acid intoxication, but that at a rate of 500 millilitres every fifteen minutes, and at lower rates in patients with liver disease or mechanical obstruction to hepatic circulation, the serum-citrate levels rose so high as to depress the ionized calcium concentration seriously. Once this had occurred, injection of calcium salts did not produce satisfactory results—the main difficulty was in asses-

[1] *Dis. Chest.*, June, 1955.
[2] *J.A.M.A.*, April 16, 1955.

sing the required amounts of calcium, and there was a very real danger of calcium overdosage. No tetany was caused in this series, although other observers have reported this complication in infants receiving replacement transfusions; but profound hypotension was in some instances observed, and was attributed to the low calcium level. The authors conclude that patients with liver disease, and those in whom surgical procedures are likely to necessitate prolonged interruption of the hepatic circulation, should preferably be given blood decalcified by passage over exchange resins or else resuspended red cells, because in these circumstances the calcium deficiency can be accurately estimated and restored. It would also seem, since the rate at which citrated blood was given had an influence, even in normal patients, on citrate retention and the lowering of calcium concentration, that when pressure transfusion is contemplated, similar precautions should be taken. This ties up with the observations of Gurd and Gardner, which were commented on in these columns on July 16, 1955; in treating hæmorrhagic shock, they found that during rapid transfusion under pressure there came a point, when some 75% of the lost blood had been replaced, at which the venous pressure rose and the arterial pressure fell rapidly; and although they attributed this phenomenon to simple overloading of the circulation, it is quite likely that Bunker and his colleagues have found the underlying explanation.

HODGKIN'S DISEASE.

DURING the last few years a series of reports has been issued from the University of California Hospital on the frequency, distribution and mortality of patients suffering from neoplastic diseases of the lymphatic and hæmopoietic tissues who were seen at the hospital from 1914 to 1951. The first report published in 1951 dealt with myeolcytic leuchæmia, the second in 1953 with lymphocytic leuchæmia, and the third in 1954 with lymphosarcoma. A fourth study has now appeared,[1] and deals with Hodgkin's disease; it is concerned with the frequency, distribution and mortality of the disease. The authors are M. B. Shimkin, K. C. Oppermann, W. L. Bostick and B. V. A. Low-Beer. It should be stated at the outset that what this report shows is that not much progress has been made in the knowledge of this disease and that the results of treatment leave almost as much to be desired now as they did more than forty years ago. G. R. Murray, writing in the first part of Volume IV of Allbutt and Rolleston's "System of Medicine", published in 1908, stated that most of the sufferers lived less than four years. It is a little better now, but not much; Shimkin and his co-authors state that the duration of illness in their series, as determined from apparent onset to death, shows no significant change during the past thirty-seven years, and this in spite of the present-day efficiency of deep X-ray therapy and the use of newer agents such as nitrogen mustard. They make a general statement of the greatest importance, but before this is set out, let us look at their findings.

The investigation covered 254 patients, and three stages of the disease were recognized. In the first stage (38 patients) the condition was localized clinically to one lymph node area; in the second stage (110 patients) involvement of two or more lymph node areas had occurred; in the third stage (106 patients) the disease had become clinically generalized beyond the lymphatic system. The peak frequency at the age at onset was in the third decade. The mean age at onset among 110 males seen through 1944 was 32·3 years and among 51 males seen after 1945 it was 33·8 years; the difference is stated not to be significant. For the females the mean age of 53 patients seen from 1914 through 1944 was 39·1 years; the mean age of 40 females seen after 1945 was 30·0 years. The difference is statistically significant and indicates the entry of younger females into the Hodgkin's population of the California Hospital centre during recent years. "The finding is unexpected and without explanation at present." Analysis of age at onset according to the three stages into which the cases were divided showed no significant differences or consistent trends that were not revealed by the sex-age scrutiny. The mean survival of the total 254 patients was 44·3 months; the five-year survival was 26·5%. When the determination was made from the date of diagnosis, the five-year survival was 18·6% for 215 patients. There was a statistically longer survival in 93 females than in 161 males; at five years after onset 36·6% of the females and 20·9% of the males were alive. Three patients remained clinically free from disease for nine to twelve years after treatment. There was no statistical correlation between survival and the age at onset. No statistically significant effect on survival could be correlated with various major forms of treatment, and nitrogen mustard was shown to produce no prolongation of life.

The conclusion of these authors has been mentioned. They point out that after many years of use of X rays in the treatment of Hodgkin's disease, the possibilities regarding dosage, frequency of treatment, type of treatment and combinations with various drugs have not been systematically explored. The view is also expressed that the introduction of nitrogen mustard and other chemical agents has expanded and complicated the problem still further. Hodgkin's disease is too uncommon "to allow any one institution to anticipate procuring, within a reasonable period of time, enough statistically usable data for the evaluation of various forms of therapy that are now available and are being introduced". A systematic plan of study is needed, criteria have to be established by which selection of patients can be made, and a "central collation" of information should be planned and carried out. A great deal has been heard from time to time about coordination of research. It is doubtful whether the population of Australia could by itself provide worthwhile information on this rare disease, but there is no reason why data collected in this country should not be collated with information obtained in centres of greater population.

[1] *Ann. Int. Med.*, January, 1955.

NITROFURANTOIN IN URINARY TRACT INFECTIONS.

OF the nitrofurantoin ("Furadantin", "Furacin") administered to a patient by mouth, 40% appears in his urine within six hours, so that in view also of its effectiveness against *Bacillus proteus*, *Escherichia coli* and *Micrococcus pyogenes* (although it is ineffective against *Pseudomonas æruginosa*), and of the fact that it causes a minimum of derangement of the intestinal flora, it seems ideally suited for the treatment of urinary tract infections. B. A. Waisbren and W. Crowley[1] have reported their studies of the drug in this connexion. First, they investigated the resistance of *E. coli* to increasing concentrations of nitrofurantoin and streptomycin, and found that in the case of nitrofurantoin no colonies grew that were significantly more resistant than the parent strain, while with streptomycin mutants appeared that were many times more resistant than the parent colony. Next, they showed that *E. coli* may produce a nitrofurantoin-inhibiting substance analogous to penicillinase. Thirdly, they showed that nitrofurantoin was bactericidal, not bacteriostatic, in action, and commenced to kill *E. coli* in some six hours. Fourthly, they showed that nitrofurantoin has about the same level of activity as the antibiotics, at approximately the same dosage levels. Finally, clinical trials of the drug showed that it was successful in controlling various chronic urinary tract infections, and even succeeded after various antibiotics had failed. Moreover, it was generally well tolerated, and did not appear to cause any toxic symptoms beyond a little nausea or vomiting. These studies seem to indicate that here we have a useful agent for treating certain urinary tract infections.

[1] *Arch. Internal Med.*, May, 1955.

Abstracts from Medical Literature.

OBSTETRICS AND GYNÆCOLOGY.

Placental Transmission of Erythrocytes.

W. F. MENGERT *et alii* (*Am. J. Obst. & Gynec.*, March, 1955) report the results of experiments with radioactive iron and sickle-cell erythrocytes in determining the placental transmission of erythrocytes. Washed donor erythrocytes tagged with Fe^{59} were injected into pregnant women, and the authors were able to determine significant amounts of radioactivity in the blood of 25 out of 29 fœtuses. The average amount of radioactivity represented the tagged cells which would have been found in 4·4 millilitres of whole maternal blood. Two pregnant women at term were given blood from donors with sickling trait but without sickle-cell anæmia. Sickle cells were thought to be demonstrated in the blood of the fœtuses after appropriate treatment. No sickle cells were seen in the blood or umbilical cord of two fœtuses serving as controls.

Intrauterine and Neonatal Pneumonia.

D. W. PENNER and A. C. MCINNES (*Am. J. Obst. & Gynec.*, January, 1955) present a study of 71 cases of intrauterine and neonatal pneumonia in which autopsy was performed at the Winnipeg General Hospital between January, 1940, and December, 1951. The incidence of pneumonia was 11·7% among 598 subjects submitted to autopsy. Most of the pneumonias were of a diffuse, bilateral, predominately polymorphonuclear leucocyte type. In most cases positive results were obtained from culture or bacteria were found in tissue sections; the control series also had a high percentage of positive results from culture. The amniotic fluid content of the lungs did not appear to be a significant factor in ætiology. The highest incidence of pneumonia occurred in premature infants with early rupture of the membranes. To reduce the incidence, the authors suggest (i) restriction of vaginal examination to cases in which it is necessary and then under strict aseptic conditions, (ii) restriction of artificial rupture of the membranes to cases in which it is absolutely necessary, (iii) administration of antibiotics to the mother when there is early rupture of the membranes, and (iv) no mouth-to-mouth resuscitation.

Radical Hysterectomy and Pelvic Lymphadenectomy.

W. LIU and J. V. MEIGS (*Am. J. Obst. & Gynec.*, January, 1955) review 473 cases, including 244 of primary invasive carcinoma of the cervix, in which treatment was by radical hysterectomy and pelvic lymphadenectomy. The purpose of the study was (i) to analyse the clinical aspects of the operation and (ii) to review the result of surgical treatment for carcinoma of the cervix. Originally the operation was restricted to patients of good operative risk, but in recent years the low operative mortality (1·7%) has led to the inclusion of more advanced and less robust patients. Fistula formation developed in 45 cases (9%), and in 35 (78%) of these the ureter was involved. Nine patients in the series, all of whom had had radiotherapy, developed multiple fistulæ. The authors state that when a ureteric fistula develops, kidney function will be lost unless surgical intervention occurs. Operation should be performed within six to eight weeks. In only eight cases out of 35 of the present series was kidney function preserved. Thirteen of the 28 uncomplicated uretero-vaginal fistulæ healed spontaneously in between one and ten months. Of the 47 patients with corpus carcinoma operated on, lymph node metastases were present in 11. The negligible effect of pre-operative irradiation on the incidence of lymph node metastases in carcinoma of the cervix was shown when metastases were present in 24 cases out of 85 (28%), as against 64 out of 259 (25%) in which irradiation was not carried out. One hundred and ninety-three patients with carcinoma of the cervix were operated upon and followed for five or more years; 139 were in stage 1, 53 were in stage 2, and one was in stage 3. The five-year salvage rate was 75% in stage 2; in 49 of these cases lymph node metastases were present, and 17 patients (35%) were salvaged; in 144 there were no metastases and the salvage rate was 81% (116 cases).

X-Ray Visualization of the Placenta.

H. G. WATSON (*West. J. Surg.*, March, 1955) reports the results of his experience in soft tissue radiography for X-ray visualization of the placenta, a procedure of particular use in the diagnosis of *placenta prævia*. He states that the apparatus needed is available in any radiological department, and the risk to the fœtus is not of concern, as the total dosage does not exceed that of X-ray pelvimetry. Of 525 cases in which a radiological opinion was sought on the presence or absence of *placenta prævia*, in 70 cases a diagnosis of *placenta prævia* was made; in 61 of these, the diagnosis was confirmed clinically. In 455 of the 525 cases, *placenta prævia* was excluded radiologically, and in none of these cases was the patient subsequently found to have *placenta prævia*. There were 18 cases in which the diagnosis of *placenta prævia* presumed on clinical grounds was confirmed radiologically before any ante-partum hæmorrhage had occurred. In 61 cases the clinical diagnosis of *placenta prævia* was suspected; this was reported as radiologically confirmed in 19 cases, and in only two was it not subsequently confirmed clinically; in 42 cases, in all of which the patients were found subsequently not to have *placenta prævia*, the diagnosis was not confirmed. The error in diagnosis in the series was 10·5%.

Manual Removal of the Placenta.

W. O. THOMAS (*West. J. Surg.*, March, 1955) reviews two series of cases of manual removal of the placenta. The first was between 1937 and 1944, when only the sulphonamide drugs were available; there were 48 cases of *placenta prævia* in 17,940 deliveries, an incidence of one in 374 or 0·27%. The second was between 1950 and 1953, after the advent of antibiotics; there were 324 cases in 18,375 deliveries, an incidence of one in 57 or 1·8%. The morbidity due to puerperal causes was 14% (seven cases) in the first group and 1·9% (six cases) in the second group. There were no deaths. The author states that prematurity, mid-forceps deliveries, long labours and operative deliveries (mid-forceps and breech) tend to increase the number of manual removals. There was an increased incidence of hæmorrhage in both groups, but the morbidity was reduced from 20% to zero; one cause was a more liberal use of blood transfusions. Of those who had hæmorrhage 78% were transfused, but 79% were anæmic at time of discharge from hospital, showing a lack of complete replacement of blood lost mainly due to underestimation of the quantity of blood lost. General anæsthesia was associated with more blood loss than local anæsthesia. Blood loss was reduced by intravenous administration of oxytocics at the moment of delivery. Out of 24 patients with placentas described in the series as incarcerated, 14 had received intravenous injections of oxytocics with the delivery of the anterior shoulder. Earlier removal of the placenta, increased use of blood transfusions and the use of antibiotics have contributed to the improvement in morbidity—in the 1950–1953 series there were 169 patients with no morbidity or mortality who did not receive chemotherapy or antibiotics; in 62% of these the placentas were removed in less than fifteen minutes, and in 93% they had been removed by the end of thirty minutes after delivery. The author concludes that a properly performed manual removal, if done early enough (by the end of fifteen minutes), provided there are no other complications, may well obviate the necessity for either transfusion or antibiotics.

Poliomyelitis in Pregnancy.

W. J. MCCORD, A. J. W. ALCOCK and J. A. HILDES (*Am. J. Obst. & Gynec.*, February, 1955) record obstetrical experiences during a large epidemic of poliomyelitis. They discuss the incidence of poliomyelitis in pregnancy as well as the effects of one condition on the other, and analyse a series of 51 patients with poliomyelitis complicating pregnancy treated at the Winnipeg municipal hospitals during the five months July to November, 1953. The epidemic reached the proportions of 338 reported cases per 100,000 of population. Males predominated over females in the ratio of 1·3 to 1·0. There were 51 pregnant patients among 153 married women of the reproductive age. The authors consider that there is probably an increased susceptibility of pregnant women to poliomyelitis. The susceptibility did not appear to alter appreciatively during the three trimesters of pregnancy. The association of pregnancy did not appear to influence the mortality rate due to poliomyelitis. The maternal deaths (six) were due to complications of poliomyelitis rather than to complications of pregnancy. There was one death in each of the first two trimesters, with four deaths in the third trimester. The

management of respirator cases was not complicated by the presence of a pregnant uterus at term. Consideration of the effects of poliomyelitis on pregnancy suggested little, if any, influence. Seven pregnancies out of 51 were terminated by abortion, a figure somewhat higher than the usual incidence of abortion. The first and third stages of labour were not appreciably affected by poliomyelitis, but in cases in which there was low spinal paralysis assistance was usually required in the second stage. The authors did not experience difficulty in delivering patients in respirators when there were uncomplicated vertex presentations. They suggest that when obstetrical difficulties are anticipated in respirator cases, the possibility should be considered of either a Cæsarean section in the respirator or the use of an anæsthetic machine to maintain ventilation on a proper table. Fœtal wastage in the series was 14 out of 51 pregnancies. One infant died nine days *post partum* with some evidence of poliomyelitis. There was no case in which the poliomyelitis virus seemed to pass the placental barrier.

Inversion of the Puerperal Uterus.

G. J. QUIGLEY (*Am. J. Obst. & Gynec.*, February, 1955) reports 14 cases of inversion of the puerperal uterus collected from the records of three hospitals in Hamilton, Ontario, one being a personal case. The condition is defined as the accidental turning inside out of the pregnant uterus during the third stage of labour, or immediately thereafter. The author follows the classification of inversion suggested by Kellogg—namely, acute inversion which is associated with complete dilatation of the cervix; subacute inversion in which the inversion is followed by firm cervical contraction; chronic inversion in which the condition has existed for more than four weeks. He states that it has been widely held that puerperal inversion is usually due to mismanagement of the third stage of labour. Too vigorous methods of expressing the placenta by fundal pressure, traction on the cord and manual removal of the placenta are important predisposing factors. However, 50% of the reported cases were of spontaneous occurrence and not preventible. The incidence of the reported cases was approximately one in 5000 deliveries, and the mortality rate was 28·6%. The four deaths occurred during the years 1924 to 1932, prior to the liberal use of blood transfusion and antibiotics. Shock and hæmorrhage were the outstanding symptoms in all except one case. The condition was recognized and treatment commenced within three hours in 11 of the 14 cases. Treatment of the patients was as follows: 11 had immediate manual reposition on recognition; one had incision of the constricting cervix; one had vaginal hysterectomy, and one was treated by vaginal packing, the inversion not being recognized. The author states that the treatment of this rare and often fatal obstetrical emergency is influenced by variable factors such as the degree of shock and hæmorrhage, the time of recognition of the complication, the degree of cervical dilatation, the presence or absence of infection and the presence of coincidental uterine abnormality. Dimpling of the fundus should suggest the possibility of commencing inversion, and inability to palpate the fundus suprapubically should arouse immediate suspicion. The author considers that inversion of the uterus should be considered in any case of post-partum hæmorrhage, especially when deep inhalation anæsthesia has been employed.

Induction of Labour.

D. S. PATTISON (*Am. J. Obst. & Gynec.*, February, 1955) discusses indications and methods of induction of labour since this procedure became recognized medical practice in 1756. He lists 17 methods of induction but states that in modern practice only two methods are usually employed—medical induction and rupture of the membranes, employed either separately or in combination. The indications for induction of labour are still the subject of controversy and vary widely in different countries and different schools. The original indication for the induction of labour in England was cephalo-pelvic disproportion, but this is not now favoured. There is a difference of opinion concerning induction of labour for conditions such as Rh-negative mothers with antibodies, post-maturity and *diabetes mellitus*. The author discusses the indications for induction of labour under the headings of maternal indications, fœtal indications and elective indications. He states that toxæmia of pregnancy which cannot be controlled by medical treatment is the outstanding indication. Hypertensive vascular disease is treated along similar lines. Renal diseases such as glomerular nephritis, pyelitis and pyelonephritis are rare indications for induction of labour if the fœtus has passed the thirty-seventh week of pregnancy. Induction of labour is indicated in cases of lateral or marginal *placenta prævia* or of *abruptio placentæ* when the ante-partum hæmorrhage has failed to respond to conservative treatment. Induction is recommended for acute hydramnios causing distress to the patient, and also for chronic hydramnios when associated with fœtal abnormality which has been confirmed radiologically. The author prefers induction of labour at the thirty-sixth week for patients with diabetes on account of the resulting lower fœtal mortality rate. Induction is practised for post-maturity if the head is deeply engaged and the cervix effaced. If the head is high and the cervix is long and uneffaced, the patient is not considered to be at term, and expectant treatment is followed. Elective induction of labour as a convenience to the patient or the obstetrician is practised by the author, and is considered a justifiable procedure if the conditions for safe induction of labour are fulfilled, and the contraindications are fully understood.

Carcinoma-in-Situ of the Uterine Cervix.

D. G. MORTON, L. J. ZELDIS and A. MONK (*West. J. Surg.*, April, 1955) report a study of carcinoma-in-situ of the uterine cervix based on observations in 22 cases of very early cervical cancer in which the diagnosis of carcinoma-in-situ was considered and was established or was excluded. In 13 of the 22 cases there was definite but minimal invasion; three cases were considered to be carcinoma-in-situ without cervical gland involvement, three had cervical gland involvement, and three had cervical gland involvement and doubtful stromal invasion. The authors consider that vaginal smear examination is responsible for bringing to light an increasing number of very early cervical cancers. Vaginal smear cytology alone was responsible for the diagnosis of eight out of 12 such cases in this series. In these eight cases the patients had no symptoms and no suspicious clinical findings. The authors suggest that a routine vaginal smear examination should be performed on all women seeking medical advice. In order to establish or exclude the diagnosis of carcinoma-in-situ they consider it necessary to excise an adequate cone from the cervix for biopsy. Ordinary punch biopsies of the cervix are considered inadequate for diagnosis of carcinoma-in-situ. The authors enumerate and discuss the histological criteria for the diagnosis of cervical carcinoma-in-situ. They consider that many features remain uncertain: the question of invasion is difficult to interpret when there is involvement of cervical glands; the feature of cell pleomorphism is variable and is found in healing cervical erosions and in hyperplasia of pregnancy. In view of these difficulties the authors suggest that the diagnosis of carcinoma-in-situ may be an unwise one. They believe that too many cases are diagnosed as "in-situ" carcinoma. In all cases with suspected early invasion treatment is along routine lines of radical hysterectomy or full irradiation therapy. When a diagnosis of carcinoma-in-situ is established after careful study of an excised cervical cone, total hysterectomy is recommended, or amputation of the cervix may be performed in young patients desirous of childbearing. In pregnancy the authors consider it safe to watch carcinoma-in-situ until after the puerperium and reassess the condition of the cervix.

Hormone Effects on Basal Body Temperature.

R. M. PERLMAN (*West. J. Surg.*, March, 1955) presents observations on menstrual patterns and rectal basal body temperatures following the administration of various hormones and other metabolic nutrients to individuals with assorted clinical pictures. Hormones such as thyroid ("Proloid"), œstrogenic substances ("Premarin") and radioactive iodine (I^{131}) were given. Impressions from the group given "Proloid" were as follows: (i) there was lessening or obliteration of symptoms associated with dysmenorrhœa; (ii) the duration and amount of menstrual flow were reduced; (iii) abnormal intermenstrual time intervals were corrected; (iv) certain irregular monophasic curves on charts were converted to biphasic or normal curves. Radioactive iodine also tended to produce normal ovulatory cycles in abnormal cases. Injections of natural œstrogens depressed the basal body temperature. The author concludes that the basal body temperature reflects pluriglandular balance and metabolic changes affecting the thermoregulatory mechanism.

On the Periphery.

HISTORICAL RELICS IN THE MEDICAL MUSEUMS OF EDINBURGH.

EDINBURGH is a city of particular interest to medical historians, and it is therefore not surprising that the museums of the Royal College of Surgeons and the Anatomy School in the University should contain many items of historical significance. The two may well be considered together, as in several respects they are complementary.

The College museum was begun with a collection of certain rarities in 1697, but its continuous and settled history dates only from 1804. Two items remain from the early collection. Both are skeletons, and both are mounted in rosewood cases. The first, with the mummified muscles still attached, was prepared and presented by Archibald Pitcairne in 1702, and the second was donated by Alexander Monro, *Primus*, in 1718. The original catalogue (1804) of the museum of "morbid preparations", which it was then decided to form, is in existence, but no dates were assigned to the items listed; many are doubtless more than 150 years old. Rapid progress was made after the appointment in 1826 of Dr. Robert Knox as Conservator, a post which for some years he combined with his famous extramural teaching. In that year the College acquired the collection of Sir Charles Bell, the results of his diligent work at the Great Windmill School of Anatomy as William Hunter's ultimate successor. Bell's collection was "in size and quality second only to that of John Hunter", and, combined with the Wilson collection, purchased simultaneously, it numbered about 4000 specimens. By this time the museum of Dr. John Barclay, an Edinburgh lecturer, had also been obtained; it included a valuable series of specimens illustrating comparative anatomy. Once the problem of housing the museum had been solved, its development proceeded more or less uneventfully.

The Anatomical Museum at the University was founded by Alexander Monro, *Secundus*, when he presented his own and his father's collection in 1798, and its subsequent progress was largely due to Sir John Goodsir and Sir William Turner. From the anatomical viewpoint the museum is particularly noted for its extensive collections of marine mammals and human skulls, the latter chiefly acquired by Turner and including many Australian aboriginal specimens. A skull of historical significance is that of Robert the Bruce (1274-1329), placed in the museum after the grave had been opened in 1819. Two similar exhibits are a copy of the death mask of Sir Walter Scott (the original is at Abbotsford), and a cast of the mummified head of the husband of Mary Queen of Scots, the Earl of Bothwell, who is buried in Denmark. A further link with Scott is the femur and tibia of the Black Dwarf, David Ritchie ("Bowed Davie"), prototype of Elshender, an exhibit presented, wrongly sided, by the physician author of "Rab and his Friends", Dr. John Brown.

The dried and varnished dissections have maintained their condition remarkably well, and the injected specimens in particular still have an educational value. The most striking example is a preparation by the second Monro of an entire adult body, the lymphatics of which have been injected with mercury. In another series of specimens the intestinal lacteals have been similarly treated. However, it would be difficult to improve upon the elegance and precision of many of the magnificent dissections made by Charles Bell displayed in the College museum. Miscellaneous items in the Anatomical Museum include specimens illustrating diseases of the eye prepared and presented by Dr. Argyll Robertson, the skeleton of the last murderer sentenced to be hanged and dissected before this practice was terminated by the *Anatomy Act* of 1832, and a cutaneous horn removed in 1671 (lest its possessor be condemned as a witch), an attached pewter disk recording the circumstances and the names of the witnesses. Sir John Goodsir's work is fittingly commemorated by the exhibition near the entrance of a striking statue, executed by Goodsir himself, of a semi-recumbent cadaver, partially dissected. The facial expression of death is superbly portrayed: to apply the term "life-like" seems paradoxical but just.

Both museums contain good collections of Listeriana, the College devoting a small bay chiefly to a model of his ward at the old Infirmary and to several patterns of his spray. The Anatomical Museum possesses the well-known marble representation of James Syme's hand holding an ankle amputation knife (his knife is displayed at the Royal College of Surgeons, England), the accompanying description being in the handwriting of the donor, Lord Lister. Also in Lister's writing is the description of a case of osteofibroma of the lower jaw, the tumour being removed, together with much of the mandible, by Syme without the benefit of anæsthesia three years after Liston had refused to operate. The tumour, which is exhibited together with a pre-operative portrait in oils and a wooden bust, is enormous, the lips being stretched to paper thinness. A photograph thirty years later shows a very good cosmetic result, no doubt partly due to a heavy growth of beard. The Burke and Hare collection, also distributed between the two museums, forms an interesting if gruesome series of exhibits. Burke's skeleton is item number 27 in the anatomical museum catalogue, his body having been publicly dissected on January 29, 1829, by Monro *Tertius*. The College display includes a cast of his head and a pocket-book made from his tanned skin, the latter containing a newspaper account of his execution.

The College museum contains an excellent collection of surgical instruments of the last two or three centuries, with a small series of Chinese instruments and Indian eye instruments. Many, such as those which belonged to Lister, Robert Liston and J. Y. Simpson, have historical significance beyond that of the specimens themselves. A set of Robert Liston's catheters, with notes on their history, were presented by R. Scot Skirving. An important but fragile instrument, now preserved in a special glass container, is the original hypodermic syringe designed and used by Alexander Wood; last year its one hundredth birthday was celebrated, and its picture was published in *The Lancet*.[1] In addition to some of Simpson's instruments, including his wooden monaural stethoscope of relatively uncommon pattern, there is a comprehensive and well-displayed series of obstetrical forceps and other instruments. The dental section is also notable for its demonstration of the evolution of the dental key from Roman times, together with a variety of early prostheses, elevators and mirrors. Anæsthetic apparatus includes a duplicate of Squire's inhaler, as used in Liston's first operation with ether. A considerable number of other instruments, including, for example, a pewter cupping set, await the tedious work of classification and display.

Sir Charles Bell's collection forms the basis of the College museum, and it is a just tribute to add that the oil paintings of war wounds, done by Bell himself, lend it an air of uncommon distinction.

Acknowledgements.

Grateful acknowledgement is made of the courtesy and help of Mr. J. N. J. Hartley, F.R.C.S., Professor G. Romanes, Dr. H. Y. Taylor and Dr. Douglas Guthrie.

Reference.

HARTLEY, J. N. J. (1948), "The Early History of the Museum of the Royal College of Surgeons of Edinburgh", *Edinburgh M. J.*, 55: 513.

British Medical Association News.

ANNUAL MEETING.

THE annual meeting of the South Australian Branch of the British Medical Association was held at the Verco Theatre, Institute of Medical and Veterinary Science, Adelaide, on June 29, 1955, DR. IVAN B. JOSE, the President, in the chair.

MINUTES.

On the motion of Dr. J. M. Pedler, seconded by Dr. M. J. C. Muirhead, the minutes of the previous annual meeting, held on June 23, 1954, were taken as read and signed as correct.

ANNUAL REPORT OF THE COUNCIL.

The annual report of the Council was received and adopted on the motion of Dr. L. C. E. Lindon, seconded by Dr. M. E. Chinner. The annual report is as follows.

At the annual general meeting of members of the Branch held on June 23, 1954, the following officers and members of Council were elected:

President: Dr. Ivan B. Jose.

Vice-President: Dr. Graham Bennett.

Honorary Treasurer: Dr. F. L. Wall.

[1] See Leading Article, THE MEDICAL JOURNAL OF AUSTRALIA, November 28, 1953.

Honorary Medical Secretary: Dr. R. C. Angove.

Ordinary Members of Council: Group A, Dr. R. H. Elix, Dr. Rollo Greenlees, Dr. Peter W. Verco; Group B, Dr. M. C. Newland, of Naracoorte.

At the first Council meeting in the new year held on July 1, 1954, the following subcommittees were appointed:

Scientific: Dr. McKay and Dr. Verco.

National Health Service: Dr. Rieger, Dr. Mallen, Dr. Bowering and Dr. Elix.

Ethics: Dr. Rieger, Dr. Wall, Dr. Verco, Dr. Cocks, Dr. Bennett and Dr. Douglas.

Parliamentary Bills: Dr. Mallen and Dr. Rieger.

Publicity: Dr. Rieger, Dr. Mallen and Dr. Greenlees.

Library: Dr. Cocks, Dr. Angove and Dr. Dwyer.

Salaries: Dr. Mallen, Dr. Rieger and Dr. Greenlees.

Editorial Handbook: Dr. Rieger, Dr. Gartrell and Dr. Mallen.

Medico-Pharmaceutical Liaison Committee: Dr. Elix, Dr. Bowering and Dr. Rieger.

Tuberculosis Standing Committee: Dr. Cowan, Dr. Hayward, Dr. Hetzel, Dr. Sutherland, Dr. Sleeman and Dr. Woodruff.

The President, Immediate Past President (if any), the Vice-President, the Honorary Treasurer and the Honorary Medical Secretary are ex-officio members of all committees other than the Ethics and Standing Committees.

The President and Honorary Medical Secretary are ex-officio members of the Ethics Committee and of all standing committees.

Attendances at Council and committee meetings were as set out in table below.

Dr. W. M. Irwin attended nine meetings of the Council in his capacity of local representative of THE MEDICAL JOURNAL OF AUSTRALIA.

Dr. J. M. Dwyer attended two meetings of the Library Committee held on September 7, 1954, and March 1, 1955. In addition to the above, two conferences with representatives from the Faculty of Medicine were held on July 8 and September 29, 1954, respectively, in reference to the question of private beds in the Queen Elizabeth Hospital, Woodville.

Two conferences with representatives from the honorary staffs of the Royal Adelaide, Adelaide Children's, Queen Victoria and Queen Elizabeth Hospitals in reference to "financial assessment of patients at public hospitals" were also held on December 9, 1954, and May 19, 1955.

Monthly Scientific Meetings.

Eight scientific meetings have been held during the year, the following programme being carried out:

1954.—July 29: Lecture by Professor Astwood, Research Professor of Medicine at the Tufts Medical School, Boston. "Medical Treatment of Thyroid Diseases and Recent Developments in Thyroid Physiology." This lecture was arranged by courtesy of the Post-Graduate Committee in Medicine. September 30: Paper by Dr. C. T. Piper entitled "Hay Fever for the General Practitioner". Discussion opened by Dr. C. C. Jungfer. October 28: Paper by Dr. J. V. Gordon entitled "Clinical Aspects of Electroencephalography". Discussion opened by Dr. T. A. R. Dinning. November 9: Special film evening when film entitled "Two Years Old Goes to Hospital" was screened. Introductory remarks by Dr. W. A. Dibden. November 25: Paper by Dr. L. O. S. Poidevin entitled "Routine Ante-Natal Care". Discussion opened by Dr. Graham Bennett.

1955.—February 25: Clinical meeting at Adelaide Children's Hospital. May 5: Listerian Oration delivered by Sir Alexander Murphy entitled "The Hasty Heart". May 26: Lecture by Colonel W. D. Refshauge, D.G.M.S.-Elect, "The Medical Aspects of Atomic Warfare".

In addition to the above, members were also invited to an open meeting of the South Australian State Committee of the Royal College of Obstetricians and Gynæcologists held on November 11, 1954, to a clinical meeting arranged by the Australian Laennec Society (South Australian Branch) held on April 14, 1955, and to the Anstey Giles Lecture delivered by Mr. J. G. B. Muir, of Hobart, at the South Australian State annual meeting of the Royal Australasian College of Surgeons held on May 20, 1955, and to a clinical meeting of the South Australian Branch of the Australasian Association of Psychiatrists held on June 7, 1955.

Membership.

The membership of the Branch is now 816 and the number of student associate members is 50. It is with regret that the following deaths are recorded: Dr. F. J. A. Juttner, Dr. G. H. Burnell, Dr. P. F. Leitch Hussey, Dr. W. E. Stevens, Dr. S. R. Hecker, Dr. H. R. R. Hancock, Dr. A. Kyle Gault, Dr. C. F. Pitcher, Dr. R. A. Goode and Dr. D. T. M. Hayes.

Representation.

Medical Board of South Australia: Dr. C. O. F. Rieger (Acting Chairman).

Dental Board of South Australia: Dr. W. John Close.

Flying Doctor Service of Australia, South Australian Section: Dr. J. M. Dwyer.

Federal Council of the British Medical Association in Australia: Dr. L. R. Mallen and Dr. C. O. F. Rieger.

Federal Medical War Relief Fund (Local Committee of Management for South Australia): Sir Henry Newland, Sir Brian Swift and Dr. E. F. West.

Saint John Ambulance Association: Dr. H. H. Hurst.

Local Representative of "The Medical Journal of Australia": Dr. W. M. Irwin.

British Medical Hall Company, Limited: Dr. C. O. F. Rieger, Dr. F. L. Wall and Dr. B. S. Hanson.

Mothers' and Babies' Health Association: Dr. R. N. C. Bickford.

Advisory Council on Health and Medical Services: Dr. L. R. Mallen.

ATTENDANCES AT COUNCIL AND COMMITTEE MEETINGS.

	Council.	Scientific.	Salaries.	Ethics.	National Health Service.	Library.	Hospital Standing Committee.
ANGOVE, R. C.	11	1	2	1	1	—	1
BENNETT, G. L.	11	1	2	3	..	..	..
BOWERING, O. W.	12	..	..	..	..	..	..
COATES, J. R.	11	..	..	..	..	..	..
COCKS, A. S. DE B.	12	..	..	1	..	..	..
DOUGLAS, S. J.	12	..	2	3	1	—	1
ELIX, R. H.	12	..	..	..	1	..	..
GREENLEES, R.	12	..	2	..	..	..	1
JOSE, I. B.	12	1	2	3	1	..	..
MALLEN, L. R.	11	..	2	..	1	..	1
MCKAY, D. G.[1]	9	1	..	..	..	..	..
NEWLAND, M. C.	9	..	..	..	..	..	..
RIEGER, C. O. F.	10	..	2	1	1	..	..
VERCO, P. W.	12	1	..	2	..	..	..
WALL, F. L.	11	1	2	3	1	..	..
Meetings held up to June 2, 1955	12	1	2	3	1	2	1[2]

[1] Leave of absence from April 1, 1955.

[2] Also Dr. R. G. de Crespigny and Dr. J. R. Magarey.

Nurses' Board of South Australia: Dr. R. L. Thorold Grant.

University Post-Graduate Committee in Medicine: Dr. L. R. Mallen, Dr. R. C. Angove and the President *ex officio*.

Central Council of the Association, London: Dr. Myles Formby.

Chiropody Board of South Australia: Dr. Neville P. Wilson.

Florence Nightingale Memorial Committee: Dr. Mary Burnell and Dr. Barbara Russell.

Australasian Medical Publishing Company, Limited: Sir Henry Newland, Dr. L. R. Mallen and Dr. C. O. F. Rieger.

World Medical Association: Dr. L. R. Mallen.

Annual Representative Meeting, London, June, 1955: Dr. D. G. McKay and Sir Philip Messent.

Joint Annual Meeting, Toronto, June, 1955: Dr. B. S. Hanson.

Sections for Special Branches of Medical Knowledge.

Section of Anæsthetics.

Report for 1954-1955.—The Section meets alternate months and is open to all members of the British Medical Association interested in anæsthesia. Present membership is 26. Much time was spent on discussion about anæsthetic positions in the various public hospitals in attempts to give adequate anæsthetic services and suitable training to students and resident staffs. The Section records with regret the deaths of Mr. G. H. Burnell, a good friend, and Dr. Stewart Hecker. At the October meeting Messrs. C.I.G. (South Australia) presented a movie film of modern obstetric management, photographed at the Melbourne Women's Hospital. At the December meeting Dr. A. D. Lamphee gave a travel talk. On March 16, 1955, Dr. John Gillies, of Edinburgh, was guest of honour at a dinner held at Mount Osmond Golf House, followed by an informal discussion. At the annual general meeting held on May 6, 1955, the office-bearers were reelected, namely: Chairman, Dr. John Barker; Vice-Chairman, Dr. John Stace; Secretary-Treasurer, Dr. Howard Ellis.

Section of Clinical Medicine.

Annual Report for the Year 1954-1955.—Membership: There are 77 members on the roll, of whom 39 are financial for the year—a decrease of three over the last year. Officers: At the annual general meeting on May 11, 1954, the following officers were elected: Chairman, Dr. C. B. Sangster; Honorary Secretary and Treasurer, Dr. A. Kerr Grant; Committee, Dr. J. McPhie, Dr. H. G. Rischbieth, Dr. I. M. H. Camens. Clinical meetings: Four clinical meetings were held throughout the year in the Physiotherapy Department of the Royal Adelaide Hospital on the second Tuesdays of May, August and November, 1954, and February, 1955. All meetings took the form of presentation of cases and the opening discussion was limited to ten minutes. All members of the Branch were circularized with a notice prior to the meeting on November 16. This resulted in attendance of 45 compared with the average for the year of 30 members for the other three meetings. British Medical Association Prize (Section of Clinical Medicine): The following two points have been decided by the Section: (i) That the value of the prize shall be left at £10 10s. (ii) That the winner of the prize for the previous year shall be officially presented at the annual general meeting of the Branch by the President of the Section, after the President has been introduced to the meeting by the President of the British Medical Association. (iii) The prize for 1954 was won by Mr. A. O. Robertson. Amendment: The annual report for 1953-1954 was amended at the clinical meeting on August 16, 1954, so that the winner of the British Medical Association Prize for 1953 should read as Mr. R. G. Wyllie, not Mr. R. G. Posen, as stated in the report.

Ear, Nose and Throat Section.

The annual general meeting was held at the rooms of Dr. R. M. Glynn on Tuesday, March 30, 1954. Three cases were shown, and the following officers were elected. Chairman, Dr. R. H. von der Borch; Vice-Chairman, Dr. A. S. de B. Cocks; Committeeman, Dr. S. Pearlman; Secretary and Treasurer, Dr. R. N. Reilly; Auditor, Mr. F. C. W. Dobbie. Three ordinary general meetings were held during the year. On Tuesday, May 25, 1954, a clinical meeting was held at the rooms of Dr. R. N. Reilly. Four cases were shown. Dr. P. G. Jay was elected Secretary and Treasurer. The post became vacant with Dr. Reilly's departure for post-graduate study abroad. On July 27, 1954, a meeting was held at the rooms of Dr. R. M. Glynn. One case was shown, and Mr. T. A. R. Dinning read a paper entitled "Neurosurgical Problems Associated with Diseases of the Ear, Nose and Throat". At this meeting a motion was carried favouring the abolition of the Ear, Nose and Throat Section of the South Australian Branch of the British Medical Association and the formation of a State Section of the Oto-Laryngological Society of Australia (British Medical Association) in its stead. On November 2, 1954, at the rooms of Dr. R. H. von der Borch, Mr. Gordon Aitchison gave a lecture-demonstration on hearing aids. The Secretary notified the meeting that the South Australian Branch of the British Medical Association had given approval to terminate the existence of the Ear, Nose and Throat Section and for the transfer of its funds to the proposed State Section of the Oto-Laryngological Society of Australia (British Medical Association). The activities of the former Section ceased as from March 7, 1955. The average attendance at meetings was seven.

Section of Ophthalmology.

Eight meetings were held during the year. Membership was fifteen and the average attendance at meetings was eleven. The annual general meeting was held on March 8, 1955, when the following officers were elected: Chairman, Dr. Charles Swan; Vice-Chairman, Dr. D. W. Brummitt; Honorary Secretary and Treasurer, Dr. J. H. Slade; Committeeman, Dr. F. J. B. Miller; Auditor, Mr. F. C. W. Dobbie. In all 28 cases were shown and discussed at meetings. On May 11 Professor Robson delivered a paper on anticoagulants. On November 9 Dr. Charles Swan gave a demonstration of microscopic slides of ocular pathology. On September 28 a special meeting was held to discuss means of obtaining assistance at the Royal Adelaide Hospital for refractions. On October 26 a special meeting was held at which guests were Mr. Nutt, of Sheffield, and Mr. Doggart, from London. Members of the Section of Anæsthetics, South Australian Branch of the British Medical Association, were invited to this meeting. Mr. Nutt showed films and delivered papers on (*a*) the sterilization of instruments by dry heat and ultra-violet light and (*b*) hibernation anæsthesia. Dr. John Barker opened the discussion of the paper and film on hibernation anæsthesia. Mr. Nutt then showed three further films on operative technique on squints. At the remainder of the meetings most of the time was devoted to the examination and discussion of cases.

Affiliated Local Associations of Members.

South Eastern Medical Association.

Four meetings were held during the year. These were as follows:

July 24, 1954, at Penola. A clinical meeting was followed by dinner, after which Mr. Grayton Brown gave an address on "The Management of Peptic Ulceration", illustrated with slides. By invitation Dr. McCann, Deputy Director of Health for South Australia, also outlined the history, progress and problems of the national health scheme.

October 23, 1954, at Mount Gambier. A clinical meeting followed by dinner, after which Dr. C. T. Piper gave a talk on "Allergy in General Practice".

January 22, 1955, at Naracoorte. A clinical meeting followed by dinner, after which Dr. Ronald MacIntosh gave a talk on "Obstetrics in General Practice".

April 16, 1955, at Mount Gambier. This was the annual general meeting when the following officers were elected: President, Dr. H. R. N. Oaten; Vice-President, Dr. M. C. Newland; Honorary Secretary and Treasurer, Dr. W. M. Moore; Committee, Dr. J. E. Dunn and Dr. D. Jorgensen. A clinical meeting was followed by dinner, and an address was given by Dr. Wallace Jolly, his subject being "Pædiatric Surgery with Special Reference to its General Practitioner Aspects". In addition, a refresher course week-end was held on June 19 and 20, 1954, when the visiting lecturers were Dr. J. E. McCartney, Dr. Mark Bonnin and Dr. R. G. de Crespigny. There are 25 financial members of the Association and the average attendance was 15 members.

Upper Murray Medical Association.

The Upper Murray Medical Association held three post-graduate week-ends and two local meetings during the past year. There was an average attendance of six members.

In March, 1954, at the Loxton Hospital the following visitors spoke: Dr. F. H. Beare, "Psychological Problems Associated with General Practice"; Dr. C. T. Piper, "Allergic Disorders: The Diagnosis and Treatment"; Dr. J. R. Magarey, "Abdominal Surgery in Relation to General Practice".

At the Barmera Hospital in June, Dr. A. S. de B. Cocks, Dr. M. T. Cockburn and Dr. A. C. McEachern were the

visiting lecturers. Dr. A. S. de B. Cocks, "Ear Diseases More Commonly Found in General Practice"; Dr. M. T. Cockburn, "The Care of the Premature Infant"; Dr. A. C. McEachern, "Pre-Operative and Post-Operative Surgical Attention".

In September, 1954, at the consulting rooms of Dr. Hayes and Dr. Kohler, of Berri, the programme was: Dr. R. M. MacIntosh, "Hormone Therapy in Gynæcological Disorders"; Dr. A. G. Campbell, "Chemotherapy of Malignant Disease"; Dr. M. E. Chinner, "Arthritis and Related Disorders".

An ordinary meeting was held at Dr. Miller's consulting rooms at Waikerie in October, 1954, at which Dr. F. B. McCann, Deputy Director of Health for South Australia, gave a summary of the present government health services. Particular reference was made to the Pharmaceutical Benefits and the Pensioner Benefits Regulations.

The annual general meeting was held in April, at the consulting rooms of Dr. Samuel and Dr. Auricht at Loxton. The following officers were elected for the following year: President, Dr. R. T. Auricht; Vice-President, Dr. T. Kohler; Secretary, Dr. R. L. Miller; Immediate Past President, Dr. W. J. Sleeman. Discussion took place regarding the setting up of a private pathological laboratory at Renmark and the suggestion for future post-graduate lectures and bi-monthly meetings.

Northern Medical Association.

Four meetings were held during the year.

The first was at Riverton on August 8, 1954, when thirteen members attended. Dr. Dwyer spoke on medico-legal problems of country general practice and Mr. T. Cleland spoke on some legal aspects of death certification.

The second was held at Blyth on November 14, 1954, when Dr. T. K. McLarty spoke on acute eye conditions. Dr. F. G. T. Turner spoke on treatment of acute dermatoses. Fifteen members attended.

The third was a post-graduate meeting held at Clare on February 20, 1955. Sixteen members attended. The lecturers were: Dr. W. J. Betts, "Some Aspects of Backache"; Dr. G. W. E. Aitken, "Functional Uterine Hæmorrhage"; Dr. H. G. Rischbieth, "Neonatal Problems"; Dr. F. B. McCann, "The National Health Service".

The fourth meeting was held at Port Pirie Hospital on May 15, 1955. Nine members attended. A film evening entitled "Rehabilitation at Mount Breckan" was shown by courtesy of the Social Services Department. This was followed by the annual general meeting when the following office-bearers were elected: President, Dr. K. Burdon; Vice-President, Dr. V. Potter; Past President, Dr. G. Wien Smith; Secretary, Dr. C. C. Dewar; Auditor, Dr. K. J. Basedow; Committee, Dr. L. R. Mallen and Dr. F. D. Rowe.

The death of Dr. H. R. R. Hancock, of Hamley Bridge, during the year is recorded with regret.

Official Visitors to "Newland House".

His Excellency the Governor of South Australia (Air Vice Marshal Sir Robert George, K.C.V.O., K.B.E., C.B., M.C.), who had previously accepted the office of Patron of the Branch, paid an official call to the Branch headquarters on December 2, 1954. He was accompanied by Captain Douglas-Scott. His Excellency was introduced to members of Council by the President and refreshments were served. The Honourable the Premier of South Australia (Mr. T. Playford) and the Honourable the Chief Secretary (Sir Lyell McEwin) called at the Branch headquarters on April 7, 1955, where they were introduced to Council members and to past presidents of the Branch, who were also invited on this occasion.

The cocktail party for 1954 was also held at the new Branch premises for the first time. The new graduates for 1954 were entertained at afternoon tea in the Council chamber on Wednesday, December 8, and the dinner to the Listerian Orator for 1955 (Sir Alexander Murphy) was also held in the committee room on May 5, 1955.

Schedule of Medical Fees: Workers' Compensation Cases.

Following negotiation with the Fire and Accident Underwriters' Association of South Australia, an increase in the medical fees payable by insurance companies for consultations and visits for workers' compensation cases came into force as from January 1, 1955. The agreement now provides for the following fees: first visit, 17s. 6d. at home or hospital, 15s. at surgery; second visit, 15s. at home or hospital, 12s. 6d. at surgery; third and subsequent visits, 15s. at home or hospital, 12s. 6d. at surgery. This represents an all-round increase in consultation and visit fees, although fees for other procedures have remained unaltered.

Prescribing of Pharmaceutical Benefits.

Throughout the year members were advised that there had been no change in the policy of the Association towards the use of government forms for use in prescribing pharmaceutical benefits and were strongly urged to use their own private forms when prescribing medicines under the provisions of the *National Health Act*.

Pensioner Medical Service.

After first having sought the opinion of the respective Branches of the Association as to the future of the Pensioner Medical Service and in view of the fact that the present agreement with the Government expired on December 31, 1954, the Federal Council accepted the offer of the Prime Minister to come to Canberra to discuss the future of the service with him and the Minister for Health.

A special meeting of the Federal Council was held at Canberra on October 28, 1954, when certain proposals of the Government regarding the future of the service were discussed, and the Government was later informed that, subject to certain provisos, these proposals were acceptable to the medical profession pending the implementation of other arrangements.

The General Secretary of the Federal Council (Dr. J. G. Hunter) addressed members of the South Australian Branch on the subject of the Pensioner Medical Service on October 21, 1954.

SOUTH AUSTRALIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION (INCORPORATED).

Income and Expenditure Account for the Year Ended December 31, 1954.

1953. £		1954. £ s. d.
2,063	To Staff Salaries and Superannuation	2,053 7 0
243	„ Postages	261 2 1
248	„ Stationery and Printing	542 6 0
58	„ Telephone and Telegrams	30 10 11
127	„ Rent	189 2 0
7	„ Legal Expenses	14 14 8
15	„ Audit and Accountancy	15 15 0
257	„ General Expenses	273 18 6
136	„ Entertainment	82 2 0
36	„ Depreciation	106 12 6
850	„ Net Surplus for Year	617 1 10
		£4,186 12 6

1953. £		£ s. d.	£ s. d.	1954. £ s. d.
6,751	By Gross Subscriptions			6,901 18 0
5,026	City	5,390 19 9		
1,641	Country	1,427 15 3		
84	Students	83 3 0		
2,782	*Less* Deductions			2,826 12 3
1,206	„ British Medical Association, London	1,170 2 9		
397	„ The Medical Journal of Australia	339 10 0		
	„ Federal Council:			
729	Capitation Fee	866 19 6		
450	„ Library Grant	450 0 0		
3,969	„ Net Subscriptions			4,075 5 9
66	„ Interest			86 0 7
6	„ *Pharmaceutical Benefits Act* Prescription Pads			25 6 2
				£4,186 12 6

The rates for attendance were increased from 9s. and 11s. to 10s. per surgery consultation and 12s. per domiciliary visit as from November 1, 1954.

Standing Committee on Hospitalization Problems.

At a meeting of the Branch Council held on April 7, 1955, a Standing Committee on Hospitals was formed with the object of investigating matters pertaining to hospitalization and with a view to increasing the number of available beds to members of the community.

This is essentially a long-range project. It is hoped that by conferring with the boards of management of some of the larger private metropolitan hospitals and taking a more active interest in their problems that ways and means may be found both to expand existing facilities and to actively assist them in raising finance with a view to the erection of additional hospitals. In common with other parts of the world, the present shortage of private hospital accommodation in this State is very acute. It does not follow that hospital building must be deferred until staff is available. The need for more and better private hospitals is an urgent matter. The Council can give a clear indication of how many more hospital beds or new hospitals are needed to serve the community adequately, and the extent to which the established hospitals need improvement in medical facilities for efficiency.

Financial Assessment of Patients in Public Hospitals.

Two conferences with representatives from the honorary staffs of the four main metropolitan public hospitals have been held throughout the year. The subject was the necessity of introducing some form of "ability to pay" to patients occupying public beds in public hosiptals. At the

SOUTH AUSTRALIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION (INCORPORATED).

Balance Sheet as at December 31, 1954.

LIABILITIES.	£ s. d.	£ s. d.
Sundry Creditors		194 2 6
General Fund:		
Balance, January 1, 1954	6,248 5 6	
Add Net Surplus for Year	617 1 10	
Add Transfer from Building Fund	1,131 17 0	
		7,997 4 4
		£8,191 6 10

ASSETS.	£ s. d.	£ s. d.
Fixed Assets—at Cost, *less* Depreciation:		
Furniture and Plant	1,599 2 6	
Delineascope and Projector	6 11 6	
Lister Medals and Dies	2 0 0	
		1,607 14 0
Current Assets:		
British Medical Hall Company, Limited, Shares at Cost—192 Preference, 134 Ordinary	3,297 10 0	
Australasian Medical Publishing Company, Limited, at Cost:		
5% Debentures	30 0 0	
3½% Debentures	1,900 0 0	
Advance not yet converted	30 8 1	
		5,257 18 1
Stocks on Hand	356 3 0	
Sundry Debtors	515 12 7	
		871 15 7
Cash at Bankers *et cetera*:		
National Bank	24 12 2	
Commonwealth Savings	200 1 1	
Savings Bank of South Australia	227 5 9	
Savings Bank Library	1 17 6	
Cash in Hand	2 8	
		453 19 2
		£8,191 6 10

Special Funds and Investments.

	£ s. d.	£ s. d.
Listerian Oration Fund:		
Balance, January 1, 1954	428 2 1	
Add Net Income for Year	9 5 5	
		437 7 6
Frank S. Hone Memorial Fund:		
Balance, January 1, 1954	662 10 9	
Add Donations and Interest	26 2 1	
		688 12 10
Trent Champion de Crespigny Memorial Fund:		
Balance, January 1, 1954	266 1 3	
Add Donations and Interest	7 13 1	
		273 14 4
British Medical Hall Building Fund:		
Balance, January 1, 1954	1,424 2 0	
Add Interest, Dividends and Donations	712 17 11	
	£2,136 19 11	
Less Transfer General Fund	1,131 17 0	
		1,005 2 11
		£2,404 17 7

	£ s. d.	£ s. d.
Listerian Oration Investments:		
Electricity Trust Debentures	310 0 0	
Savings Bank of South Australia	127 7 6	
		437 7 6
Frank S. Hone Memorial Fund:		
Commonwealth Bonds, 3¼%, 1959	50 0 0	
South Australia Gas Debenture	300 0 0	
Electricity Trust Debenture	250 0 0	
Savings Bank of South Australia	88 12 10	
		688 12 10
Trent Champion de Crespigny Memorial Fund:		
Savings Bank of South Australia		273 14 4
British Medical Hall Building Fund:		
Commonwealth Bonds, 3½%, 1960	200 0 0	
Savings Bank of South Australia	491 7 11	
Commonwealth Bank General Account	313 15 0	
		1,005 2 11
		£2,404 17 7

F. C. W. DOBBIE, Secretary. F. L. WALL, Honorary Treasurer.

We hereby report that we have examined the Books and Accounts of the South Australian Branch of the British Medical Association, Incorporated, for the year ended December 31, 1954. In our opinion, the above Balance Sheet, together with the Statements of the Special Funds, are properly drawn up so as to exhibit a true and correct view of the affairs of the Branch, as at the above date according to the best of our information, the explanations given to us, and as shown by the Books produced.

Adelaide,
May 2, 1955.

ANNELLS, TILLEY, HUNWICK AND COMPANY,
Chartered Accountants (Aust.).

present time there is no "financial assessment" of any in-patients at the Royal Adelaide Hospital, although a flat rate of 2s. is charged for each out-patient visit.

The consensus of medical opinion holds firmly to the belief that patients who are members of voluntary insurance organizations, those covered under workers' compensation, third party risk, and patients who have sufficient means to pay fees should no longer continue to receive treatment from members of the honorary staff who are not remunerated in any way for their services.

Although members of the medical profession have always considered that there is a moral obligation on them to render a free service to deserving sections of the community, it has never been their intention to provide a service for all and sundry irrespective of any ability to pay.

One of the main objects of the National Health Scheme is to relieve the strain on public hospital accommodation by encouraging people to seek advice from their local doctor and by assisting them to meet the cost of private medical and hospital care. It is considered that its object will be defeated unless some form of financial assessment is imposed on persons seeking admittance to public hospitals, a large proportion of whom it is well known can afford to pay for private treatment.

Your Council is fully alive to the anomalies of the present system and strong representations have been made to the Government on several occasions.

Medical Certification.

Several matters in connexion with medical certification have occupied the attention of the Council throughout the year following receipt of complaints against the members concerned. The practice of issuing a medical certificate which is misleading or untrue is a serious matter from the legal point of view, and leads to a lowering of the prestige of the medical profession in the eyes of the public.

Members have been urged to exercise great care and responsibility when issuing a medical certificate within the limits of professional secrecy, and to resist demands for certificates which are sought on other than legitimate medical grounds.

Federal Council of the British Medical Association in Australia.

Three meetings of the Federal Council have been held throughout the year, namely: Brisbane, August 30 to September 1, 1954; Canberra, on October 28, 1954; and in Melbourne on February 14 to 16, 1955. The South Australian Branch was represented at these meetings by Dr. L. R. Mallen and Dr. C. O. F. Rieger.

London House.

During the year the Branch Council raised the sum required of it on a *pro rata* to membership basis, and a cheque for £110 was subsequently forwarded to the Federal Council of the British Medical Association in Australia by whom the London House Fund was inaugurated.

Frank S. Hone Clinical Prize.

The Frank S. Hone Memorial Prize, which was awarded on the results of the December, 1954, examinations for the degrees of Bachelor of Medicine and Bachelor of Surgery, was won by Solomon Posen.

Honorary Life Membership.

Dr. R. G. Burnard, Dr. Phoebe Chapple, Dr. Rupert E. Magarey, Dr. Helen M. Mayo and Dr. J. MacBain Ross all completed fifty years' continuous membership of the Association at the end of 1954 and have thus become honorary life members of the Association. The Council desires to congratulate these members on this achievement.

Honours and Awards.

The Council tenders its congratulations to Sir Darcy Cowan and to Sir Archibald John Collins, President of the Federal Council of the British Medical Association in Australia, on the bestowal of the honour of Knight Bachelor by Her Majesty the Queen, to Sir Henry S. Newland, who was awarded the Gold Medal of the British Medical Association on April 13, 1955, "in recognition of his outstanding services to the Association and the medical profession", and to Dr. Gilbert Brown, O.St.J., and Dr. Frank Mugford, C.St.J., who have been promoted in the Venerable Order of St. John of Jerusalem.

The Council is most appreciative of the work of the Secretary (Mr. Dobbie) and the Assistant Secretary (Mr. Stephens) throughout the past year. There has been a marked increase in the volume of work since the office of the Branch was moved to Brougham Place. One of the reasons for this is that members are finding the new address more accessible.

(Signed) IVAN B. JOSE, President.

FINANCIAL STATEMENT.

The financial statement, which is printed herewith, was adopted on the motion of Dr. F. L. Wall, seconded by Dr. C. O. F. Rieger.

ELECTION OF OFFICE-BEARERS.

In the absence of other nominations, Dr. Ivan B. Jose declared Dr. G. L. Bennett duly elected as President of the Branch for the ensuing twelve months and invested him with the badge of office. Dr. Bennett thanked the members for his election.

Dr. Bennett announced the election of the following office-bearers for the ensuing year:

Vice-President: Dr. M. E. Chinner.

Honorary Treasurer: Dr. F. L. Wall.

Honorary Medical Secretary: Dr. Ronald Hunter.

Members of Council: Group A—Dr. M. T. Cockburn, Dr. I. A. Hamilton, Dr. C. C. Jungfer. Group B—as no nomination had been received for Group B, the incoming Council, in accordance with the rules, would fill the vacancy at its first meeting.

On the motion of Dr. F. L. Wall, seconded by Dr. C. O. F. Rieger, Messrs. Annells, Tilley, Hunwick and Company were appointed auditors for the ensuing year.

PRIZE FOR CLINICAL MEDICINE.

The chairman of the Section of Clinical Medicine, Dr. F. Ray Hone, presented to the President and to Dr. Ivan Jose, the retiring President, Mr. Tony Robertson, who had been awarded the Section's Clinical Medicine Prize in September, 1954. Dr. Bennett congratulated Mr. Robertson and Dr. Jose presented him with a certificate of the award.

AMENDMENT OF BY-LAWS.

Dr. G. L. Bennett stated that two new by-laws had been drafted by the Council during the year, and in accordance with Rule 75 the Council now sought the approval of members to their adoption. Copies had previously been circulated to all members with the annual report.

The Secretary read the new By-Law 40 as follows:

> 40. Members shall protect as far as lies in their power the practice of a deceased member for a period of six months after the date of death and if the practice is sold during that period then for a further period of six months after the date of the sale and shall discourage as far as possible patients endeavouring to transfer from the deceased's practice.

It was explained that the principle underlying this rule was that the deceased's executors should be able to sell the practice at a fair price and should have a reasonable opportunity to find a buyer. And the purchaser should be protected as he could not secure a personal introduction.

On the motion of Dr. Sholto Douglas, seconded by Dr. L. R. Mallen, it was unanimously resolved that the new by-law should be approved and incorporated in the rules and by-laws of the Branch.

The Secretary then read the new By-Law 36A as follows:

> 36A. No member shall conduct his professional practice through or by means of a limited liability company if any of the shares of the company or any interest in any such shares are or is held by or on behalf of or in trust for any person who is not a legally qualified medical practitioner.
>
> Even though the whole of the issued shares of a limited liability company are bona fide held by legally qualified medical practitioners for their own benefit, the conduct of his practice by a member through or by means of such company is considered to be undesirable and contrary to the interests of the profession as a whole because it is detrimental to the establishment and maintenance of a proper relationship between the practitioner and his patient.

Dr. P. L. Verco moved and Dr. O. W. Bowering seconded the motion that the new by-law should be approved and incorporated in the rules and by-laws of the Branch. After discussion of an amendment approving the first part and suggesting modification and further consideration of the second part, the motion was put to the meeting and carried.

RETIRING MEMBERS OF COUNCIL.

On the motion of Dr. M. T. Cockburn, seconded by Dr. C. C. Jungfer, a vote of thanks was carried to retiring members of the Council: Dr. A. S. de B. Cocks, Dr. O. W. Bowering, Dr. D. G. McKay, Dr. Coates, Dr. R. Angove and Dr. Sholto Douglas.

RETIRING PRESIDENT'S ADDRESS.

Dr. Ivan Jose then read his retiring president's address (see page 317).

Dr. Thorold Grant proposed and Dr. Ian Hamilton seconded a vote of thanks to Dr. Jose for his address. The vote was carried with acclamation, and Dr. Jose replied.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

FAMINE AT SYDNEY COVE.[1]

[From "A Narrative of the Expedition to Botany Bay", by Watkin Tench, Captain of Marines.]

ON the 6th of May the Supply sailed for Lord Howe Island to take on board turtle for the settlement: but after waiting there several days was obliged to return without having seen one, owing, we apprehended, to the advanced season of the year. Three of the transports also which were engaged by the East India Company to proceed to China to take on a loading of tea sailed about this time for Canton.

The unsuccessful return of the Supply cast a general damp on our spirits, for by this time provisions were becoming scarcer than in a blockaded town. The little live flock that with so heavy an expense and through so many difficulties, we had brought on shore, prudence forbade us to use: and fish, which on our arrival and for a short time after had been tolerably plenty were become so scarce, as to be rarely seen at the tables of the first amongst us. Had it not been for a stray Kangaroo which fortune now and then threw in our way we should have been strangers to the taste of fresh meat.

Thus situated, the scurvy began its usual ravages and extended its baneful influence, more or less, through all descriptions of persons. Unfortunately, the esculent vegetable productions of the country are neither plentiful nor tend very effectually to remove this disease. And the ground we had turned up and planted with garden seeds, either from the nature of the soil, or, which is more probable, the lateness of the season yielded but a scanty and insufficient supply of what we stood so greatly in need of.

Correspondence.

THE MEDICAL SERVICES OF THE AUSTRALIAN ARMY.

SIR: It arouses many happy memories to read the forthright remarks of Dr. (Lieutenant-Colonel) T. J. Ritchie (M. J. AUSTRALIA, August 6, 1955) and to find that "The Bondi Doctor" is as active and thoughtful as he was amongst the sandhills of El Alamein.

The reluctance of many young medical graduates to train in the Royal Australian Army Medical Corps is symptomatic of the post-war spirit that besets this country, a wishful forgetting of past horrors and future dangers, in spite of all warnings. There is no sense of urgency, even in the minds of some whose studies were carefully protected by the sacrifice of others, and who yet protest that they have "had the war". Nor will recruiting be stimulated by making uniforms and training more attractive, safe, easy and comfortable. *Esprit de corps* is born of action, not of self-esteem.

It was the same in the years before the recent war. It was always the minority who were keen, and until the sense of urgency began to sink in after Munich, the numbers were small and the attitude was stagnant. But after Munich, young men of a much brighter and keener type came along, for the brief period that was allowed to them.

Training in tactics and administration takes time, and experience is necessary for effective command, although leadership of men is a gift which depends largely on strength of character. Not that length of peace-time service always brings a proportionate advantage (except in seniority). Some of our most detestable obstructionists during the war had shown considerable prowess in the Militia. The supreme test of our efficiency was to win the respect of the fighting soldier. This is not realized by those who are absorbed in academic pursuits and imagine that a medical officer is synonymous with a doctor in uniform.

There are fewer Citizen Military Forces medical units now than there were before the recent war in which to train; and the reserve of officers is a kind of military vacuum, though not a sufficient vacuum to prevent rust. It remains, as Dr. Ritchie has said, for those of us who have had experience in war or in the post-war Citizen Military Forces to arouse by all possible means that spirit of obligation that will encourage the few to become the leaders of the future. But our minds must not be fixed in the past. Let us do all we can, by training, by example, by encouragement, by keeping ourselves alert and in touch with post-war tactical problems; but not, please, by the spectacle of former colonels and brigadiers strutting round their hospitals, clothed in a little brief authority.

Yours, etc.,

14 Parliament Place,
Melbourne, C.2,
August 9, 1955.

W. W. LEMPRIERE.

RESERPINE IN THE TREATMENT OF CHRONIC MENTAL PATIENTS.

SIR: As an addendum to Dr. Bower's investigation into the use of reserpine in the treatment of chronic mental patients (published in the issue of July 16, 1955), it was thought useful to make a further small study. In order to determine the significance of selection in treatment-response eight males were chosen from the large number of deteriorated schizophrenics in the chronic wards of this hospital. Collectively the group exhibited the whole range of schizophrenic symptomatology, but no patients were included in the trial who showed persistent "overt verbal and motor aggression", as did those in Dr. Bower's investigation. Reserpine dosage, oral and intramuscular, was the same, but electro-convulsive therapy three times weekly was added in order to evaluate the effect of combined therapy. No other special attention was given, and the interest of the staff and patients in "the new drug" was not stimulated unduly. Although treatment was continued for four weeks, none of the patients showed any significant improvement. This would seem to support the conclusion that reserpine is of limited use in selected patients only, and that it is no panacea for the rehabilitation of the mentally sick.

Yours, etc.,

Mental Hospital,
Beechworth,
Victoria.
August 3, 1955.

L. A. GUILE.

THE RESERPINE ANTI-HYPERTENSIVE DRUGS.

SIR: Dr. Swanton has done well to draw attention to the dangers of reserpine. There must be very few drugs which have "no known contraindication", and reserpine is certainly not one of them. Furthermore, in many patients it has no hypotensive effect and leads only to intolerable dreams, depression, a stuffy nose and feelings of unreality. In doses more than 1·0 milligramme a day reduction of blood pressure is usually not much greater than with doses less than 0·5 milligramme a day, but the side effects are much more severe.

[1] From the original in the Mitchell Library, Sydney.

It is quite clear that no anti-hypertensive drug yet discovered is a causal prophylactic, and the mode of action of all of them is to interfere with vascular homœostasis. For that reason one has to be very sure of the necessity for treatment before embarking on a regime which may prove uncomfortable and will almost certainly have to be followed for the rest of the patient's life. In no disorder is prognosis more difficult than in high blood pressure; indeed, there is no unanimity when high blood pressure is present, and this is particularly true in so-called mild hypertensives who are stated to do best with rauwolfia preparations. It is quite certain that an arbitrary definition of 140/90 for the upper limit of normal, however convenient for administrative purposes, is positively dangerous if applied to the whole population regardless of age, build, sex, temperament, habits, heredity and coincident vascular disease. Symptoms, unless they be due to the complications of hypertension, are of no help, for one doubts seriously whether hypertension *per se* produces any symptoms. Those that are found in association with benign hypertension are usually psychogenic or menopausal and respond as often as not to phenobarbitone. One has seen the same symptoms in aortic coarctation completely unrelieved by successful resection. There is at present no evidence that reduction of the blood pressure in benign uncomplicated hypertension interferes in any way with the process which over the years progressively raises the peripheral resistance; it may do so, but we do not know. If it does not, then nothing would be gained by treating hypertension before the symptoms of complications appear. We have seen enough of surgical sympathectomy to know that considerable statistical ingenuity is required to prove that it prolongs the life of uncomplicated hypertensives. Until properly controlled studies are made over ten to twenty years information on the efficacy of rauwolfia and other hypotensive drugs in prolonging the life of asymptomatic and mild hypertensives is equally uncertain.

Because of this uncertainty the writer does make an exception in young people below forty years of age with unequivocal hypertension, for here the prognosis is known to be bad and the loss of a parent in a child's formative years may well prove catastrophic.

Once complications of hypertension have occurred, we are on more certain ground, and if the patient can tolerate them, which with proper care is nearly always, the prognosis in malignant hypertension and in heart failure is much better than formerly. Here rauwolfia preparations have their place, but the very multiplicity of hypotensive drugs and the potentially unpleasant side effects of every one of them make the successful treatment of complicated hypertension much more difficult and time-consuming than the treatment of diabetes. Successful management demands considerable judgement and experience.

There is very little information available on the natural history of hypertension in general as opposed to hospital and consulting practice. May I suggest, sir, that the new College of General Practitioners begin an inquiry into this matter using modern statistical methods. In ten or twenty years the profession would then have some solid facts to guide them in their management of hypertension. The cost of such an investigation to the community would be far less than the amount spent in the last three years on hypotensive drugs.

A general practitioner friend of mine has two letter boxes at his front gate. Under the one marked second class mail, which is bottomless, is an open galvanized-iron receptacle. Once a week the contents are removed by the local council. One wonders whether his moderately hypertensive patients fare any worse than those of others treated with all the resources of modern science.

Yours, etc.,

143 Missenden Road,
Camperdown,
New South Wales.
August 8, 1955.

R. B. BLACKET.

Research.

SIR DAVID WILKIE RESEARCH FELLOWSHIP IN SURGERY AND/OR MEDICINE.

THE Dean of the Faculty of Medicine, University of Edinburgh, has advised that the David Wilkie Research Fellowship in surgery and/or medicine, of the value of £800 to £900 (sterling) *per annum*, with a possible allowance for

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED AUGUST 16, 1955.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	3(2)	7(5)	3(2)	..	..	..	..	..	13
Amœbiasis	..	..	..	..	1(1)	..	..	..	1
Ancylostomiasis	..	..	..	..	..	..	..	..	..
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	..	..	..	..
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	1	10(10)	2(2)	..	..	..	..	..	13
Diphtheria	1	3(2)	4(3)	..	3(2)	..	..	..	11
Dysentery (Bacillary)	..	3(2)	3(3)	4(4)	19(19)	..	..	..	29
Encephalitis	1	..	..	1(1)	..	..	..	..	2
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	31(11)	56(25)	..	23(11)	2(1)	..	2	..	114
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	2	..	..	..	..	..	2
Malaria	..	..	2	..	..	..	12	..	14
Meningococcal Infection	4(2)	5(4)	1(1)	1(1)	1	..	..	..	12
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	4(2)	3(2)	1(1)	1(1)	..	..	..	..	9
Puerperal Fever	..	..	..	..	..	..	..	..	..
Rubella	..	25(14)	..	4	5(4)	..	..	..	34
Salmonella Infection	..	..	..	..	..	..	..	..	..
Scarlet Fever	8(7)	21(10)	40(14)	3(2)	2(2)	..	..	..	74
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	1	..	..	..	..	..	..	1
Trachoma	..	..	..	..	2	..	..	..	2
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	41(29)	26(15)	26(18)	7(4)	13(7)	1	2	..	116
Typhoid Fever	..	..	..	..	1(1)	..	..	..	1
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	2(2)	..	..	..	2
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

approved expenses of research, and tenable for two years (with possible extension to three years at the discretion of the Senatus Academicus), will be open for award in October, 1956. The Fellowship is open to graduates of any university. The holder will be required to carry out approved research work in surgery and/or medicine in the University of Edinburgh, and he must attend the honours class in physiology, unless he is already a graduate in physiology or in science. While undertaking the research work he will be expected to maintain contact with clinical work, but the time to be devoted to this will be restricted to two half-days per week. During his tenure the Fellow will not be permitted to study for or to present himself for any examination leading to a higher diploma in medicine or surgery.

Applications must be submitted on a prescribed form, a copy of which may be obtained from the Dean of the Faculty of Medicine, or from the Chairman, National Health and Medical Research Council, Department of Health, Canberra, A.C.T., Australia, to whom applications should be sent by October 31, 1955.

Naval, Military and Air Force.

APPOINTMENTS.

THE undermentioned appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Numbers 33 and 34, of July 14 and 21, 1955.

CITIZEN NAVAL FORCES OF THE COMMONWEALTH.

Royal Australian Naval Reserve.

To be Surgeon Commander.—Surgeon Lieutenant-Commander David Norman Livingstone Seward.

Royal Australian Naval Volunteer Reserve.

To be Surgeon Commander.—Surgeon Lieutenant-Commander Graeme Lindsay Grove.

AUSTRALIAN MILITARY FORCES.

To be Honorary Physician to the Queen.—Colonel William Dudley Refshauge, O.B.E., M.B., B.S., M.R.C.O.G., Royal Australian Army Medical Corps, *vice* Major-General Frank Kingsley Norris, C.B., C.B.E., D.S.O., E.D., M.D., F.C.N.A.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Professor D. R. MacCalman.

THE following programme in the annual subscription course has been arranged for Professor D. R. MacCalman:

Tuesday, September 20, 8.15 p.m., at the Stawell Hall, 145 Macquarie Street, Sydney (in conjunction with the Kindergarten Union of New South Wales): "Preventive Psychiatry."

Friday, September 23, 8.15 p.m., at Broughton Hall Psychiatric Clinic: Lecture to psychiatrists in the Department of Health.

Professor Robert Platt.

The following programme in the annual subscription course has been arranged for Professor R. Platt:

Wednesday, September 21, 12 noon, at the Maitland Lecture Theatre, Sydney Hospital: A talk on "Hypertension" and presentation of cases.

Friday, September 23, 2 p.m., at the Students' Lecture Theatre, The Royal North Shore Hospital: Presentation of cases.

Friday, September 23, 8.15 p.m., at the Stawell Hall, 145 Macquarie Street, Sydney: "The Metabolic Effects of Renal Disease."

Nominations and Elections.

THE undermentioned have applied for election as members of the South Australian Branch of the British Medical Association:

Murchland, John Byrne, M.B., B.S., 1954 (Univ. Adelaide), Hamley Bridge, South Australia.

Brown, Maurice William, M.B., B.S., 1953 (Univ. Adelaide), 24 Park Terrace, Gilberton, South Australia.

Diary for the Month.

AUG. 29.—Queensland Branch, B.M.A.: Bancroft Oration.
SEPT. 3.—Queensland Branch, B.M.A.: Annual Meeting.
SEPT. 6.—New South Wales Branch, B.M.A.: Organization and Science Committee.
SEPT. 7.—Victorian Branch, B.M.A.: Clinical Meeting.
SEPT. 7.—Western Australian Branch, B.M.A.: Branch Council.
SEPT. 9.—Tasmanian Branch, B.M.A.: Branch Council.
SEPT. 13.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
SEPT. 19.—Victorian Branch, B.M.A.: Finance Subcommittee.
SEPT. 20.—New South Wales Branch, B.M.A.: Medical Politics Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all contract practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rate is £5 *per annum* within Australia and the British Commonwealth of Nations, and £6 10s. *per annum* within America and foreign countries, payable in advance.